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CONTENTS OF VOLUME II

JULY, 1911. NUMBER 1

PAGE
The Treatment of Sepsis in Scarlatina with Antistreptococcus Serum. Matthias Nicoll, M.D., New York 1
Accessory Sinus Suppuration in Scarlatina. Thomas Hubbard, M.D., Toledo, O. 11
Studies in the Metabolism of Atrophic Infants. Charles A. Fife, M.D., and Borden S. Veeder, M.D., Philadelphia 19
A Preparatory Study of the Bacillus Acidophilus in Regard to Its Possible Therapeutic Use. Thomas Morgan Rotch, M.D., and Arthur I. Kendall, Ph.D., Boston 30
Anaphylaxis in Its Relation to Pediatrics. Godfrey R. Pisek, M.D., and Marshall C. Pease, M.D., New York 39
The Fundamental Requirements of an Infant's Nutrition. John Howland, M.D., St. Louis 49
Progress in Pediatrics 55

AUGUST, 1911. NUMBER 2

The Occurrence of Infantile Paralysis in the United States and Canada in 1910. Robert W. Lovett, M.D., Boston 65
The Cerebral Forms of Poliomyelitis. Henry Koplik, M.D., New York .. 75
Infantile Paralysis: Spinal Form. John Lovett Morse, A.M., M.D., Boston 92
The Control of Epidemic Poliomyelitis. Simon Flexner, M.D., New York 96
Infantile Paralysis. The Most Promising Outlook for Improvement in Treatment from the Standpoint of the Pediatrician. J. H. M. Knox, Jr., M.D., Baltimore 102
The Rôle of Mineral Salts in the Metabolism of Infants. B. Raymond Hoobler, M.D., New York 107
Progress in Pediatrics 141

SEPTEMBER, 1911. NUMBER 3

A Case of Scaphocephalus with Retinal Changes. Arthur Willard Fairbanks, M.D., Boston 149
Muscular Hypertrophy of the Pylorus in Infancy. Henry Larned Keith Shaw, M.D., and Thomas Ordway, M.D., Albany, N. Y. 159
Albumin-Milk in Infant Feeding. Clifford G. Grulee, M.D., Chicago .. 180
Protein Metabolism in Infants and Children. Herman Schwarz, M.D., New York 189
A Case of Infection of the New-Born. Louise Tayler-Jones, M.D., Washington, D. C. 210
Progress in Pediatrics 212

CONTENTS OF VOLUME II

OCTOBER, 1911. NUMBER 4

PAGE

Epidemiologic and Etiologic Studies of Acute Poliomyelitis in Pennsylvania. Samuel G. Dixon, M.D., Harrisburg 221

Relationship of Gastric to Pancreatic Fat Digestion in Infants. J. P. Sedgwick, M.D., and F. W. Schlutz, M.D., Minneapolis 243

Hippuric Acid in the Urine of Normal Breast-Fed Infants. Samuel Amberg, M.D., and J. H. Mason Knox, Jr., Baltimore 248

Further Observations on the Acid Control of the Pylorus in Infants. David Murray Cowie, M.D., and William Lyon, M.D., Ann Arbor ... 252

The Relation of Meat Ingestion to Indicanuria in Children. E. Charles Fleischner, M.D., San Francisco 262

The Treatment of Chronic Nephritis in Children by the Edebohls Operation. Henry Koplik, M.D., New York 267

Progress in Pediatrics 281

NOVEMBER, 1911. NUMBER 5

A Discussion of Mikulicz' Disease with Report of a Case of Lymphatic Leukemia in a Child with Marked Enlargement of the Salivary Glands. Wilder Tileston, M.D., New Haven, Conn. 293

A Study of the Caloric Needs of Premature Infants. Julius H. Hess, M.D., Chicago 302

The Use of Malt Sugar and High Percentages of Casein in Infant Feeding. John Lovett Morse, M.D., Boston 315

A Note on the Bacteriologic Examination of Lymphatic Glands in Scarlet Fever. John Albert Kolmer, M.D., Philadelphia 329

The Intestinal Infantilism of Herter. R. G. Freeman, M.D., New York. 332

Myatonia Congenita: A Report of a Case with Autopsy. W. T. Councilman, M.D., and Charles Hunter Dunn, M.D., Boston 340

Progress in Pediatrics 356

DECEMBER, 1911. NUMBER 6

Infantile Paralysis with Especial Reference to Its Occurrence in Massachusetts, 1907-1910. Robert W. Lovett, M.D., and Mark W. Richardson, M.D., Boston 369

Pyloric Stenosis in Older Children, with Report of a Case of Pyloric Spasm Ending Fatally. Edwin E. Graham, A.B., M.D., Philadelphia 407

An Apparatus for the Collection of the Excreta of Infants. Eugene F. DuBois, M.D., New York 415

A Metabolism Bed for Infants. John Howland, M.D., St. Louis, and Robert A. Cooke, M.D., New York 419

Progress in Pediatrics 422

American Journal of Diseases of Children

VOL. 2 JULY, 1911 No. 1

THE TREATMENT OF SEPSIS IN SCARLATINA WITH ANTISTREPTOCOCCUS SERUM

MATTHIAS NICOLL, M.D.
NEW YORK

In using the term sepsis in scarlet fever I desire to be understood as referring to a set of clinical symptoms occurring forty-eight hours or longer after the onset of the disease, which are apparently due to the invasion of the body by organisms of the streptococcus group, which, up to the present time, are not known to possess any cultural or other characteristics which serve to distinguish them from streptococci isolated from a number of other morbid conditions. The symptoms may be briefly stated as follows: No fall of temperature, or a renewed rise; abnormal swelling of the mucous membrane of the throat, with or without superficial sloughing; profuse nasal discharge; marked cervical adenitis; rapid, often irregular pulse; mental apathy; active or low delirium. Streptococci may or may not be found in the blood, and it should be said that while they are usually present in prolonged cases especially, they are not necessarily so, even in those which must be clinically regarded as septic and, on the other hand, may be found at an early stage in cases whose course is otherwise benign and which do not admit of other than a technical diagnosis of this condition.

Until the organism which causes scarlet fever has been definitely determined we must continue to regard those cases which are overwhelmed by the onset of the disease and are likely to succumb in twenty-four to forty-eight hours as directly due to this undetermined cause. Such are, in this country at least, of comparatively infrequent occurrence. The greater number of severe and fatal cases being of the class the symptoms of which I have described.

Scientific workers on the problem of scarlet fever seem more and more inclined to disregard the possibility, formerly so generally advocated, of streptococci representing anything more than the invasion of a secondary organism on a soil suitably prepared by some unknown agent. If this view proves to be correct, it must be confessed that certain well-authenticated phenomena are thus rendered most difficult of explanation. Of these I may mention the undoubted success of vaccination with killed streptococci from scarlet fever patients as a means of preventing the latter. This work has been largely confined to Russia and apparently has caused but little interest in this country. Of the recent reports I may mention that of Tesjakoff, who in a study of 15,000 vaccinated patients, reaches the conclusion that three inoculations extending over two weeks is able to protect against the disease. Again Raíkowa, making observations in seven epidemics, on 721 vaccinated patients, found that among 524 patients vaccinated but once nine cases of scarlet fever occurred; among 122, vaccinated twice, five cases, while seventy-five patients vaccinated three times remained free from the disease.

Verhoff points out that the death-rate in 403 vaccinated patients in whom scarlet fever occurred was but 6 per cent., compared with a rate of 17.5 per cent. in the unvaccinated. Furthermore, all those who have made use of vaccination, from Gabritchewsky, who originated it, to the present, agree as to the common occurrence in those inoculated, of symptoms which cannot be distinguished from those of scarlet fever of the milder type as regards the onset, course, rash and occasional complications. Again, if the streptococcus be eliminated, how are we to account for the good results of the antiserum in Moser's fourth category of cases —those patients overwhelmed by the first rush of the disease—which showed a mortality of 100 per cent. without serum, and 65 per cent. or less with its use?

Two recent attempts to do away with the streptococcus as a causative factor are of interest. Cantecuzène, of Bucharest, reported to the Société de Biologie in April, 1911, that he had inoculated nine of the lower monkeys with bronchial glands, pericardial exudate and blood, the latter two free from streptococcus, taken from scarlet fever patients, and produced what appeared to be in all respects true scarlet fever, having an incubation period of seven to thirty-five days, and followed by typical desquamation. I am authorized by Dr. William H. Park to state that six monkeys (*Macacus rhesus*) injected with the blood of six different scarlet fever patients not tested for streptococcus, failed to show any symptoms of the disease, one dying after a few days of ileocolitis. Dr. George Bernhardt of Berlin, working under Gaffky, reported in April that by inoculating a number of lower monkeys with suspensions of tongue-scrapings, serum and enlarged nodes of scarlet fever patients, subsequently excising the enlarged inguinal nodes near the site of injection, grinding and passing the latter through other monkeys, he was finally able to procure nodes showing no streptococcus or other organism, whose further inoculation into another series of monkeys caused symptoms in all respects similar to those in scarlet fever of human beings.

If this work can be confirmed, it must be conceded that the streptococcus can no longer be regarded as the causative factor or essential to its development. Until this is accomplished it would seem wise to have an open mind on the subject, especially as it is becoming daily more evident that with greater refinement of technic and newer methods of differentiation, we may soon be able to assign to the various strains of these organisms specific characteristics in the production of different morbid conditions, one of which may be scarlet fever.

The serum treatment of scarlet fever, first brought into prominence by Moser, whose name is usually associated with a serum produced by the inoculation into horses of streptococci taken from many patients with scarlet fever, was, like most specific remedies, hailed at first with the greatest enthusiasm, and, like most specifics, the results obtained did not fulfil popular expectations. If one consults the now fairly voluminous literature on the subject, he is sorely puzzled to account for the contradictory opinions set forth as to the worth of the serum. This, in part, is to be explained, I believe, by difference in the methods of its employment, whether used early, or only late, in moribund cases; differences in the type of the disease, not only locally, but as between different countries; and finally, by judgment founded on too few cases. There is, furthermore, undoubted difference in the antitoxic strength of sera and not unnaturally a prejudice against the use of the huge doses which seem essential to the production of results.

I shall refer to but one set of observations, those of Fedinski of Moscow, published in 1910, who in a most elaborate analysis of 317 cases in which serum was used, compared with about 900 cases without it, comes, as it seems to me, to the very reasonable conclusion that the serum given in full doses before the fifth day greatly increases the chance of recovery, even in the apparently hopeless cases; that in a large majority the temperature falls by crisis within twenty-four hours, or, if by lysis, the course of the fever is shortened. The occurrence of complications is less frequent and their gravity diminished. The influence on the heart's action, central nervous system, the rash and on necrotic processes is marked. The dosage in the average severe case was 200 c.c. subcutaneously, except in the case of young children, when 100 to 150 c.c. were given, and this dose was repeated in from twenty-four to forty-eight hours if necessary. Chart 1 shows the deaths from scarlet fever in the City of Moscow for a series of years. The solid line represents those patients who died outside the hospital, the dotted line those receiving hospital treatment. It will be noted that the average of the hospital deaths held well above those dying in the city, but that with the beginning of serum treatment in the hospitals, and especially in the second year of its use when others than the apparently hopeless patients were thus treated, the hospital patients show a death-rate well below those treated outside and without serum.

In this country the serum treatment of scarlet fever has, as far as I know, been but little tried. My own experience was obtained at the Scarlet Fever Hospital of the Department of Health of New York City during February, March and April, 1910, in the course of a very extensive epidemic of the disease. The serum used was that prepared under the direction of Dr. Park, consisting of eleven strains of streptococci from scarlet fever patients—blood, throat, glands, etc., and one of streptococcus from a case of endocarditis. Owing to a somewhat limited supply at the time, it was thought advisable to give but 50 c.c. as an initial dose, which of course precludes the possibility of comparison with the European results. In so far as was possible in a badly overcrowded hospital, with overworked staff and nurses, every patient who showed markedly grave symptoms, regardless of the day of disease, was injected by the staff or myself and visited by me daily, with the exception of four cases furnished me by the resident physician. By no means all the fatal cases during these months were the patients injected, as measles, diphtheria and other complications accounted for their unfavorable progress and often death. Again, patients who, in spite of the severity of onset, seemed to be in no immediate danger, not infrequently took so sudden a turn for the worse that there was no opportunity to make use of the serum.

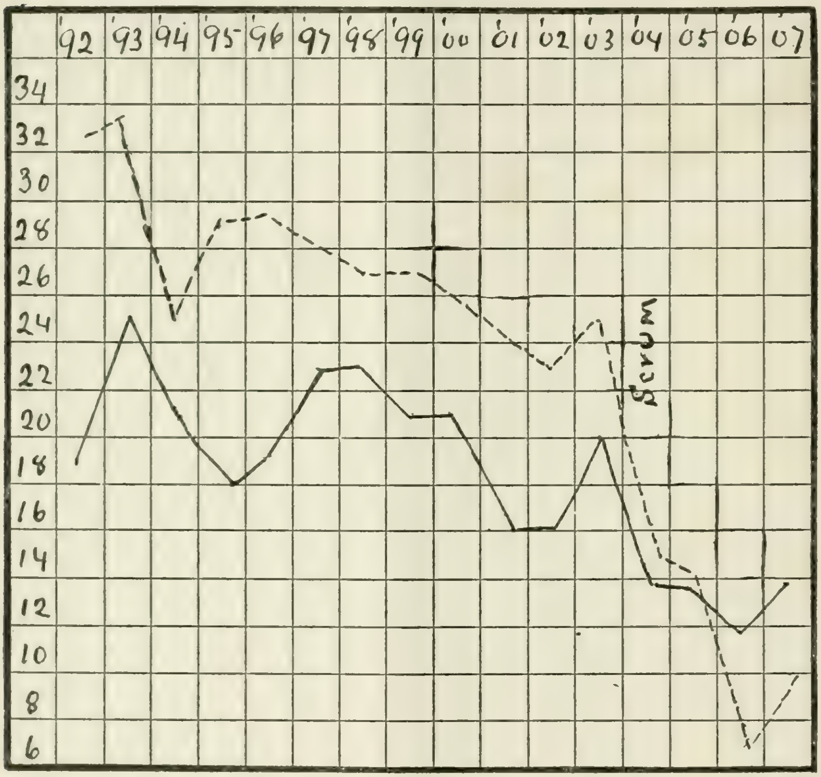

Chart 1.—The solid line shows the mortality curve from scarlet fever in Moscow from 1892 to 1897; the figures on the left show the percentage; the dotted line shows the mortality in the Vladimir-Kinderhospital during the same period under serum treatment.

There were injected in all, thirty patients, of whom seventeen died; not a very brilliant showing, it must be confessed, but on analyzing the fatalities, the poor results may be reasonably accounted for without detracting from the value of the serum. Of these seventeen cases, four patients were brought in the hospital in a moribund condition, immediately injected, and died within a few hours. Of those who were ward patients twenty-four hours or longer, one died within two hours after receiving injection, two others within twelve hours, a length of time too short to hope for any relief from a subcutaneous injection. Another patient, after seeming to respond favorably, contracted measles and ileocolitis; another measles, followed by gangrenous varicella. The condition of three others was shown to be due to a complicating diphtheria which failed to yield to large doses of antitoxin following the serum. One patient was injected late in the disease, with the hope of affecting a double mastoiditis, 100 c.c. being given intravenously. The result was inconclusive, as an operation was thought desirable. Following this, the patient received 100 c.c. subcutaneously, grew gradually weaker, with no marked lowering of the temperature, which had been exceedingly high, and died two weeks later in extreme emaciation. This leaves four patients in whom the failure of the serum must be accounted for on other grounds than those just described.

Case 1.—H. H., aged 7, had been ill three days on admission; temperature 104.2 F., pulse 144, respiration 32; glands in the neck greatly swollen; patient looked extremely septic. The patient was given 100 c.c. of serum subcutaneously, pulse, respiration and temperature falling the next day and the temperature not going much above normal until just before death. Ten days after receiving treatment, the heart action became very unsatisfactory; the patient looked very pale and weak; stimulation seemed to have no effect, the pulse growing weaker and more irregular day by day. A few days later, the patient developed general choreic movements, followed by arthritis of the left wrist, and died three weeks after admission apparently of heart failure due to myocardial involvement.

I have the records of two cases similar to this in patients who were given 150 c.c. intravenously for a very grave mixed infection with diphtheria. The local throat symptoms cleared up readily under the combined use of antitoxin and serum, but the patients both died a week or more later, one with a very rapid heart action, and the other with a pulse which fell from 120 to 53.

Case 2.—S. McB., aged 4, ill eight days; throat very much swollen; cervical nodes greatly enlarged; patient profoundly septic and delirious; temperature 104, pulse 180. The patient was given 50 c.c. of serum and died thirty-six hours later without any apparent amelioration of conditions. The failure of the serum in this case may be reasonably attributed to the length of time the patient was ill.

Following are two cases (3 and 4) in patients of Dr. Sexton, the resident physician, whom I did not see. They were, however, very carefully studied and the pulse and temperature taken every two hours, before and after the administration of serum.

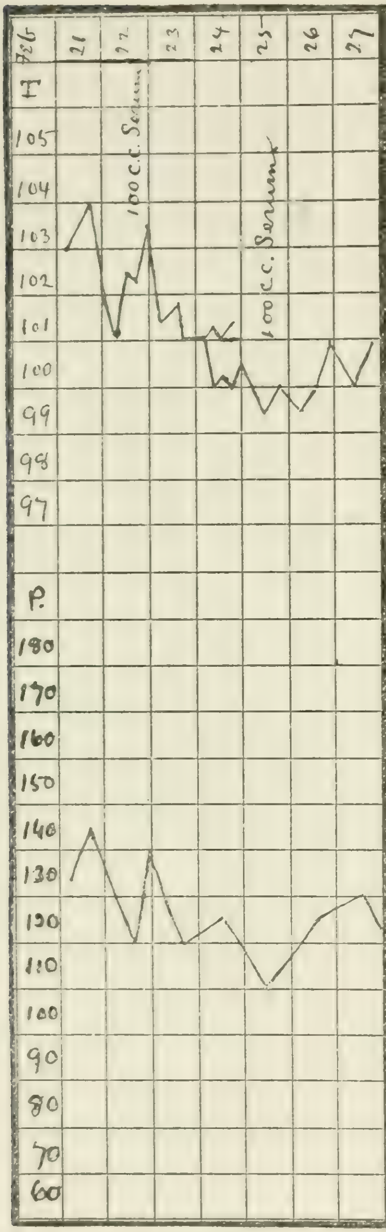

Chart 2.

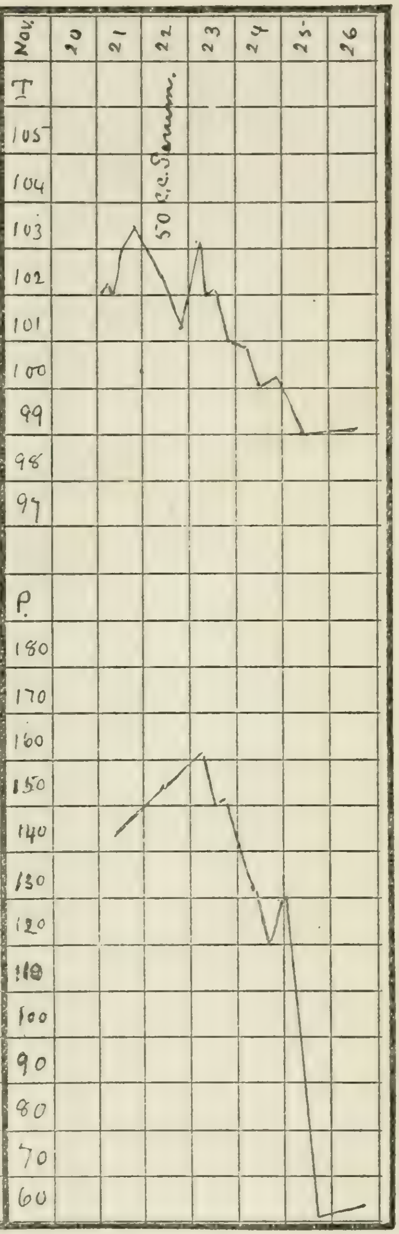

Chart 3.

Chart 2.—Shows the effect on temperature and pulse of serum administered in Case 5.

Chart 3.—Showing effect of serum treatment in Case 6.

Case 3.—J. K., aged 2, had been ill four days on admission November 17, when the temperature was 103.4 F., pulse 140, respiration 32. This condition did not change markedly during the next five days. The cervical nodes were very much swollen; the pulse at times was imperceptible. On the ninth day of her illness she was given 50 c.c. of serum and died thirty-six hours later without any appreciable effect having been produced.

Case 4.—J. M., aged 16, was admitted November 14. November 23 the temperature was 104.5 F., pulse not countable, respirations much increased. The next day when the 50 c.c. of serum was given the temperature was 101.2 F., pulse 180, respiration 144. The patient was markedly septic, cyanosed, and wildly delirious, heart sounds muffled, pulse hardly perceptible. Temperature the next day was 100 F., pulse 160 and of a better quality; respiration 36. On the second day his temperature dropped to 97 F., pulse to 104 and respiration to 36. The patient was still cyanosed and very delirious. Mouth and nose discharged profuse bloody secretions. The third day the patient was still delirious, though the pulse was of better quality. On November 28, four days after giving the serum, the temperature was 100 F., pulse 152, respiration 36. The color was better and the pulse of a fair quality. Nourishment was taken well; nose and mouth were still bleeding. Later in the day, the condition became suddenly worse; the patient became cyanotic and died of heart failure.

If the serum had been given in anything like sufficient quantities at an earlier stage in these two cases, it is possible that it might have been successful in its action.

Of the patients who recovered, a short history of a few will serve to show the apparently good effect of the serum.

Case 5.—S. K. (Chart 2), aged 10; ill two days on admission; covered with an intense dusky rash with much vesiculation; throat and cervical lymph-nodes very much swollen; lips dry and fissured; constant muttering delirium; 100 c.c. of serum given subcutaneously. The next day the temperature fell; the delirium continued. The following day, 100 c.c. serum was given. There was a general and profuse desquamation over the whole body; the patient was not delirious, but very stupid. The day following there was a marked improvement in the general condition. The subsequent history was one of convalescence, interrupted by multiple arthritis in the third week. The patient was discharged in good condition after a long stay in the hospital.

Case 6.—E. R., aged 7 (Case of Dr. Sexton). The patient had been ill six days on admission, was profoundly septic, gums and lips sloughing, teeth dropping out, eyes injected and excreting profusely, cervical nodes much swollen, patient unconscious. He was given 50 c.c. of antistreptococcus serum on the second day after admission to the hospital, when his temperature was 102.3 F., pulse 150, respiration 132. The subsequent course of his temperature and pulse is shown in chart 3.

Two days after receiving serum, the condition of the mouth and gums had very much improved. On the sixth it was noted that the patient was crying for food. On the eighth the pulse, temperature and respiration were normal and the recovery was complete.

Case 7.—L. J. (Chart 4), aged 15, had been ill two days on admission; very toxic; vomiting was constant; throat was very much swollen, also the cervical nodes; pulse very rapid and feeble. Improvement took place in twenty-four hours, with uneventful recovery, after the administration of 100 c.c. of serum, given on the third day after her admission to the hospital.

Case 8.—R. S. (Chart 5), aged 6½, ill two days. Dr. Sexton, who observed the case throughout, noted that the patient was wildly delirious, but did not regard her as septic. The temperature was 105.5 F., pulse imperceptible, respiration 44. She was given 50 c.c. of serum on her admission to the hospital; twenty-four hours later the delirium was less marked and the temperature and pulse were down. The following day the patient's condition was excellent, delirium had ceased, and recovery was very rapid.

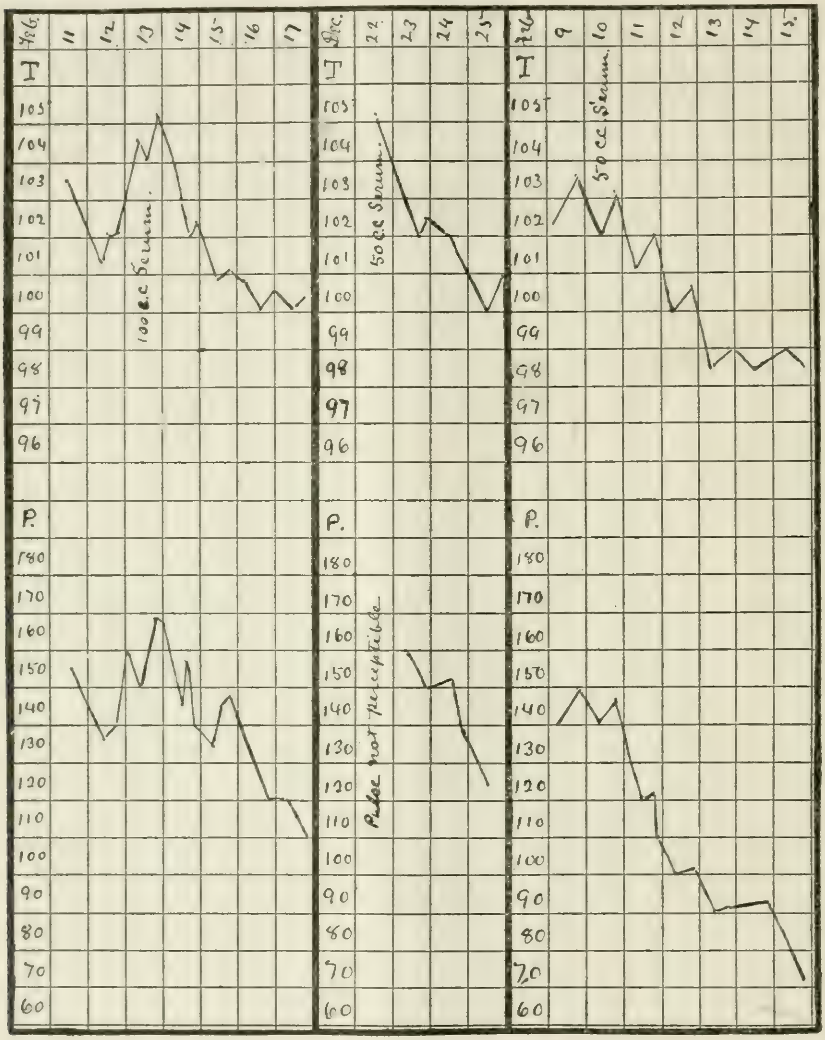

Chart 4. Chart 5. Chart 6.

Chart 4.—Effect of serum treatment in Case 7.

Chart 5.—Result of serum treatment in Case 8. Patient ill only three days.

Chart 6.—Showing drop in pulse and temperature after administration of serum in Case 9.

Case 9.—H. S. (Chart 6), aged 10, had been ill two days on admission. The patient was very septic, with swollen throat and cervical nodes. Fifty c.c. of serum was given on the fourth day of her illness. Temperature and pulse fell by rapid lysis, and recovery was uneventful.

These examples are sufficient to illustrate the apparent effect of the serum on the pulse and temperature, and on the general and local septic conditions.

In a number of other cases in which the temperature was not so high, but in nearly all of which the pulse was very rapid, the effect of the serum was marked. The following illustrates its usefulness in local conditions about the nose and throat.

Case 10.—S. K., aged 8½, had been ill five days on admission. The patient was apparently suffering from marked general sepsis, with profuse, foul, dark-colored nasal and oral discharge, with great swelling of the cervical nodes; lips also markedly swollen and fissured. The patient's mouth was wide open all the time. He was extremely apathetic. On the eighth day of his illness he was given 50 c.c. of serum, at which time the temperature was 101, the pulse 140. The amount of discharge from his nose and mouth was simply appalling. The temperature the next day rose 2 degrees; the pulse fell slightly. The following day the pulse fell to 110, the discharge showed very marked improvement and a few days later had ceased, the patient making an uneventful recovery.

What bad effects from the serum may be expected? In the foreign statistics rashes of various kinds occurred in a large number of cases, generally, however, of an urticarial type; also rise of temperature, evidently due to the same cause in about half the number, and occasionally polyadenitis, arthralgias and localized edemas. In my experience, I should say that with a dosage given subcutaneously, even of 50 c.c., an urticarial rash was the rule rather than the exception. Other and severer forms of rash I have not seen. A moderate rise of temperature accompanying the rash is not infrequent. Polyadenitis and arthralgias which could be definitely attributed to the serum were not noted. One case of true anaphylaxis occurred recently:

Case 11.—P. P., aged 5, was admitted January 28, after one day's illness with scarlet fever and diphtheria. He was given 6,000 units of antitoxin on admission, and on the following day, as his throat seemed worse, 10,000 units. The patient had a tuberculous hip joint and was in generally poor condition. His subsequent history was that of chronic sepsis, with double mastoid infection, requiring operation, and abscesses in various parts of the body which when opened healed very badly.

April 17, seventy-nine days after admission to the hospital, a blood-culture was made and immediately antistreptococcus serum was allowed to run into the same vein. It ran very slowly, not more than 10 or 15 c.c. entering the vein, when the patient, who had been whimpering, gave one or two sharp coughs and attempted to vomit. The face became intensely cyanosed, and then deathly pale, except for a purple band extending across the forehead and eyes. The needle was immediately withdrawn, and the patient put to bed. He was unconscious, his color absolutely death-like; the pulse could not be felt; a dusky erythema covered the whole front of the body. The respirations, which had previously been 38 to 40, varied from 15 to 22 a minute with deep inspiration, very noisy and drawn through closed teeth. A few minutes later a purpuric rash covered the right limb from hip to ankle, the color disappearing only under long pressure. On the inside of the left leg, was a rash somewhat scarlatiniform in character.

These rashes disappeared in half an hour, except on the inner side of the right foot, where a circinate rash took the place of the purpuric. Under active stimulation and heat, consciousness returned within an hour and the patient recognized those about him. There were râles at the bases of both lungs which had not been noted previously. The next day the pulse, temperature and respirations were about as they were previous to the injection. On the following day there was an exanthematous rash on the scalp, and a patch of erythema in front of the right ear. The subsequent history of the patient was one of progressive emaciation, death taking place about ten days later.

Whether these phenomena would have resulted from a subcutaneous injection I am unable to say. In another case, not scarlet fever, the patient developed a severe local anaphylaxis followed by an extensive area of sloughing at the point of inoculation following her eighteenth subcutaneous injection, the previous injections having caused nothing more than a mild urticaria. For this apparent lack of immunity to horse-serum, after seventeen injections given at short intervals, I have no explanation to offer, unless it is to be regarded as an example of the Arthus phenomenon. I have had an opportunity during the last few months to observe the effect of large doses of this serum given intravenously, and with the exception of the case mentioned I have not seen any alarming results which could be attributed to this method of administration. However, I am not prepared at this time to recommend its general use in this way, except in those cases in which a delay of twelve hours would probably determine a fatal outcome. Here, intravenous injections are by all means to be preferred.

Until there is some method of standardization and concentration of the serum, it would seem highly desirable to use a dosage believed to be essential to the best results by those who have had most experience with it, namely, for older children and adults, 200 c.c. injected, by preference, one-half into each side of the lower abdomen; for infants and young children, 100 to 150 c.c. in all.

The apparatus employed has been used for a number of years in the New York Department of Health for the inoculation of horses with large doses of serum, and I have found it most convenient for clinical purposes. It consists of a glass container, which may hold from 100 to 200 c.c., a rubber tube sufficiently long to be convenient, and a force pump which serves to give enough pressure to cause the serum to enter the tissues through the needle. It may be used equally well for intravenous injection. Care should be taken to see that the serum is heated to 100 F., otherwise a chill will result.

Finally, while my somewhat limited experience with this remedy does not entitle me to form a decided opinion, I cannot help but feel that in a disease over which we have little or no control, and which so frequently goes unexpectedly wrong, in all severe cases of scarlet fever, the serum, if attainable, should be made use of in full doses and without delay.

124 East Sixtieth Street.

ACCESSORY SINUS SUPPURATION IN SCARLATINA*

THOMAS HUBBARD, M.D.
TOLEDO, OHIO

As would be naturally inferred from the title, this article deals almost exclusively with the acute scarlatinal sinus suppuration of childhood. If the rhinologist of to-day is to do his whole duty he must be alive to the fact that the exanthematous diseases of childhood, and particularly scarlet fever, often present certain complications in the line of acute sinus infections that are quite as important, as concerns the immediate and future welfare of the child, as the well-understood acute ear infections.

Grünwald[1] contributes the valuable experience of a careful observer in tracing cases of chronic suppuration back to the primary cause. He includes pneumonia, typhoid fever, diphtheria, and particularly scarlet fever, as causes of the initial infections. Most of the authorities in pediatrics mention sinus suppuration (maxillary chiefly) as a complication of scarlet fever, but none of them emphasizes its importance in a manner sufficient to stimulate a proper conception of this disease process, and certainly not in the manner to put this complication in its proper place as a definite disease condition that should be studied and treated from the standpoint of a rhinologist.

We have now a better understanding of the factors that contribute to the virulency of secondary nasal diphtheria as observed in pre-antitoxin days, knowing that even in young children there are vulnerable accessory sinuses which, once invaded, add to the specific toxemia a septic condition which makes these cases so invariably fatal. I have seen this condition in scarlatina: pansinusitis, pus discharge, localized edema over frontal and orbital regions, as the chief objective symptoms progress to a rapidly fatal issue and did not label it properly as the first step toward rational treatment. Between this severe type and the so-called purulent rhinitis type, frequently seen in connection with the exanthemata, and which usually recover, but with perhaps a chronic suppuration or catarrhal condition, there is a group of cases which have well-developed sinus suppuration. These deserve careful study and special local treatment, and failing in that they may be amenable to more or less radical surgical treatment.

To begin with, we should treat the acute rhinitis of scarlet fever as a definite infection of the nasal mucosa, liable at any time to invade the sinuses and not, as the present practice prevails, chiefly with the object of preventing ear infection. Keeping this precept clearly in mind the alert rhinologist will not be surprised with a well-developed purulent sinusitis on his hands. Not that he can always prevent it, but he will not be led into taking part in a vain hunt over the whole anatomy for the cause of post-scarlatinal fever and retarded convalescence, and finally be pushed into the embarassing position of making the sinus diagnosis by exclusion. That is to say, if nothing else, it must be a suppurating sinus.

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*Read at the meeting of the American Laryngological, Rhinological and Otological Society, Atlantic City, June, 1911.

[1] Grünwald: Nasal Suppuration, 1900, 2 Ed., Wm. Wood & Co., New York.

Suppurative rhinitis *per se* is a rare condition—at least to the degree that one is quite justified in assuming that pus from the nares means purulent sinusitis. The fact that spontaneous cure occurs does not prove that the sinuses were not involved.

We are in the habit of regarding the sinuses as being anatomically unimportant in childhood. They are only in process of development from 5 to 12 years of age, the ostia are proportionately large and if infected are relatively less liable to empyema than in adults. But scarlet fever breaks many pathologic ordinances, and we certainly must learn to recognize sinus suppuration in children even though the anatomist teaches that it is improbable. The maxillary sinus and the ethmoid cells are the most constant in early childhood, but even prior to 10 years of age the frontal and sphenoidal sinuses are sufficiently large to be invaded.

Another factor in leading the rhinologist off the scent, as it were, is that he is likewise an otologist. The ear trouble is usually more in evidence at this stage and he is distracted by the danger thereby entailed and, perhaps, is attracted by the urgent surgical indications. He opens the mastoid, exenterates the process and hopes that his surgical duties are over. Usually they are, but not always. An infectious process that can penetrate to the middle ear would naturally be expected to invade cells and sinuses that are directly accessory to the mucous tract primarily invaded. All otologists can recall cases of this character in which the healing of the mastoids was very slow, and in spite of perfect ear surgery the discharge continues through the tympanic membrane, gradually destroying all chances of restoration of hearing. Unaccountable fever persists and convalescence is retarded. Sometimes this is attributable to adenoids or extensive lymphadenitis, but occasionally it is sinus suppuration. Remember that in children pus is not always in evidence unless there is ethmoid edema to the degree of blocking the flow into the throat. It must be searched for, and even then it is more diffcult to trace to its source than in the adult.

In a classical article by Killian,[2] the pathology and surgical indications are clearly presented. Killian records six cases coming under his observation and surgical treatment, in all of which the patients suffered from sinus suppuration due directly to scarlatina. Three of these were acute, and as it is this class in which we are particularly interested, a brief review of them will be given.

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[2] Killian: Die Erkrankungen der Nebenhölen der Nase bei Scharlach. Ztschr. f. Ohrenh. u. Krankh. d. Luftwege, September, 1908.

KILLIAN'S CASES

Case 1.—Boy, aged 11. On the eighth day of scarlatina severe frontal headache, local tenderness and swelling of the left orbital tissues were noted. The nasal discharge contained streptococci. Systemic symptoms indicated lung involvement and also nephritis. Local symptoms of sinus suppuration increased, with edema and tenderness over the frontal and maxillary sinus areas. Metastatic abscesses followed and the child died on the fifteenth day. The autopsy showed septic thrombosis of the superior longitudinal sinus consequent on general accessory sinus empyema, leptomeningitis and metastatic abscesses in the lungs.

Case 2.—Boy, aged 6. On the twelfth day of scarlatina tenderness and edema over the left frontal sinus and orbital edema, together with general sepsis and local pus discharge, enabled Killian to establish the diagnosis of acute frontal sinus suppuration. Later maxillary involvement was in evidence. Although the general symptoms indicated possible sinus thrombosis—superior longitudinal or cavernous—yet operation was decided on and performed by Killian on the thirteenth day of sickness. The ethmoid and sphenoid cells were explored through the orbital opening and found to contain pus and granulations. The frontal sinus, although very small, and the maxillary sinus were full of pus. Drainage was established into the nose by the removal of the anterior third of the middle turbinate and the maxillary antrum was irrigated for about two weeks through the canine fossa opening. Streptococcus serum was administered. Recovery was rather slow but complete.

Case 3.—Girl, aged 12. Operation was made in 1905 by Killian, by the intranasal method, about the forty-fifth day of scarlet fever. The principle symptoms were, pus from nares, from frontal, ethmoidal and maxillary sinuses and marked orbital edema. The diagnosis of empyema was confirmed by radiograph. The maxillary and frontal sinuses were irrigated and ethmoid cells freely opened. Two weeks later symptoms improved but the report closes with expression of doubt as to purulent discharge from the nose.

Three other cases are recorded by Killian in which suppurations of rather more chronic type, due to scarlet fever, were cured by operations by the radical method. Nineteen additional cases recorded in literature are detailed, fifteen of which were in children, the youngest being 2½ years. Of these nineteen cases, fifteen patients were operated on by the more or less complete radical method; that is, through the orbital incision. In nearly all the ethmoid cells, as well as the frontal, were cleaned out and drained, and such as had maxillary involvement were operated through the canine fossa. A few had prior or subsequent mastoid suppuration, likewise operated on. Thirteen of the fifteen patients operated on recovered; that is, only two in whom thorough operation was undertaken. died.

Detailed autopsy reports of nine cases collected from the literature are recorded by Killian. In all of these there was empyema of the accessory sinuses following scarlet fever, but in many death was not directly attributable to this complication. The important point is that accessory sinus infection is often insidious and in the presence of other grave complications the symptoms are often overlooked. Wertheim finds accessory sinus empyema in one of five autopsies of children dead of scarlet fever, and Moritz Wolf records five findings of empyema in five autopsies of children dead of scarlet fever, three of which had the scarlet fever and diphtheria type. Nineteen diphtheria autopsies by Wolf showed pus in the accessory sinuses, even though many of these patients had exhibited very slight clinical symptoms.

The complications and sequelæ of scarlet fever are so varied and grave that statistics are not of much value unless careful detailed comparisons are recorded, and of course that is impractical and unnecessary in a review of this character. The percentage of recoveries implied by Killian's statistics by no means tells the whole truth as to the mortality of accessory sinus suppuration in scarlatina. Probably many fatal cases are not diagnosed as having sinus disease, and some present no favorable opportunity warranting operation. No doubt some of the fatal operated cases are not reported. But we certainly are warranted in the conclusion that the operation is justifiable, in fact strongly indicated, in many cases presenting a very extensive and serious degree of sinus suppuration and we should include those with symptoms of venous sinus thrombosis, and that, too, with a fair chance of successful termination, even in the hazardous post-scarlatinal condition.

Killian's conclusions are very important: sinusitis is nearly always present in varying degree in the severe rhinitis of scarlatina. Sinus empyema is present in nearly all fatal cases presenting symptoms of purulent rhinitis. However, in some serious cases the discharge may be very slight. Marked intranasal edema over the ethmoid region is always present if the ethmoids are involved. The maxillary antrum is most frequently infected, and as a rule the most advanced pathologic changes are here found, but fortunately there is less danger of serious results from extension than obtains with the other sinuses.

The ethmoidal, frontal and sphenoidal sinuses are alike vulnerable to infection in proportion to their development. The ethmoidal cells are the most constant anatomically in childhood, which accounts for intranasal edema as a prominent symptom.

When we take into consideration the treacherous character of this serious disease we may expect irregular and rapid progress of the disease process. In other words the systemic forces of resistance may be overwhelmed and invasion and destruction may involve the body walls, and produce necrosis such as is often observed in scarlatinal suppuration of the middle ear and mastoid.

The essential objective symptoms of scarlatinal sinus suppuration are: discharge of pus from the naris containing pyogenic cocci, rise of temperature, local edema and tenderness of special sinus areas. Ocular symptoms are not very dependable in childhood and exophthalmos is rare. Fatal septic phlebitis or meningitis may follow sinus infection before the local symptoms have developed to such a degree as to attract attention. It must always be taken into consideration that the majority of acute infections of the sinuses subside spontaneously, but this is perhaps less true of scarlatinal sinusitis than of the ordinary type. It is doubtful if any case presenting the symptom-complex in marked degree can recover without spontaneous or artificial complete evacuation of the pus. The tendency toward bone necrosis is characteristic of scarlatinal sinusitis. The most vulnerable points are: in ethmoidal suppuration, the lamina papyracea (os planum); in the frontal sinus, the inner orbital region just above the lachrymal bone, and in the maxillary sinus, the superior wall.

Meningeal invasion is less likely to follow ethmoidal than frontal sinus empyema, probably because of the anatomic fact that there is less resistance intranasally in the former. Anatomically one can see little reason why there should not be quite as frequent dural as periosteal evidences that the inflammation has penetrated through the bony wall. Of course this observation does not apply to the muco-periosteal lining of the sinuses, since that is the seat of primary infection, but certain it is that facial edema over special areas in this serious type of acute infection should be considered a warning that the infection may be likewise progressing through the inner table. A sudden subsidence of periosteal edema may be coincident with meningeal invasion. This undoubtedly occurs in the most virulent type, and intracranial symptoms may supervene and with symptoms which so overshadow the accessory sinus symptoms that they are scarcely considered a factor in the pathologic complex of scarlatinal septicemia.

The bacteriology of scarlatinal sinus suppuration will be dismissed with a few words, as it is in a rather chaotic state and there is nothing definitely known except that pyogenic cocci are invariably found.

The age of the patients makes the ordinary intranasal operations impractical, and conditions are usually so grave that the importance of thorough radical work is essential. There is no question that the radical method—the Killian operation—modified and adapted to the acute condition, is the one to be chosen. Frontal, ethmoidal and sphenoidal sinuses should be explored, granulations and carious tissue removed, and permanent free drainage established. As a general rule a portion of the middle turbinate must be sacrificed to secure perfect ethmoid drainage, and the fronto-nasal duct should be enlarged. As previously stated, the operation must be so thorough and the drainage must be so free that after-treatment will be easy, for a sick child should not be subjected to the daily terror of painful irrigations and dressings.

REPORT OF AUTHOR'S CASE

CASE 4.—*Suppurative Sinusitis Involving Frontal, Ethmoidal, and Maxillary Sinuses, Following Scarlatina, Complicated by Suppurative Mastoiditis. Operation. Recovery.*

History.—Dec. 23, 1910, G. M. J., aged 12, developed acute tonsillitis with otitis media. The primary symptoms were very severe, with false membrane deposit on the tonsils, and a fulminating otitis. The throat culture showed streptococci. On the second day of illness two other children in the family developed scarlatina. The fact that this boy had had scarlatina when three years of age (with suppurating ears), made diagnosis by throat symptoms doubtful, but by the third day of illness he also had a well-developed rash over the chest and subsequent desquamation. Within twenty-four hours of initial ear symptoms the membrana tympani was freely incised and soon after pus flowed freely. The acute systemic symptoms subsided in a few days and thereafter his temperature was rather low for such extensive streptococcus invasion as followed. Early in the attack there was a very severe rhinitis with general edema of the nasal mucosa of both nares. It should be mentioned that there was persistent frontal headache early in the sickness but it was thought to be due to the mastoid inflammation, which is not rarely referred to this region. Sneezing was a prominent symptom. There was also marked photophobia. The gradual development of mastoiditis drew attention from the nasal symptoms, but there was a constant and copious sero-mucous discharge from both nares, which, however, did not become noticeably purulent until about the fifth week of sickness. In the meantime the ear condition progressed to suppuration in the mastoid cells, and complete mastoid exenteration was necessitated early in the third week. Fortunately there was no nephritis and no evidences of systemic disturbance followed, and for a week he did remarkably well. Frontal headache and photophobia subsided.

Then, in spite of apparently perfect postoperative conditions in the mastoid, the temperature, which had been near normal for a week, began to show a daily rise of 1 or 2 degrees. There was no discharge from the ear; in fact, hearing became normal ten days after operation and the patient progressed to complete healing of the mastoid in three weeks. The daily rise of temperature was coincident with the appearance of a mucopurulent nasal discharge from both nares. During the early period of the mucopurulent discharge from the nares there were no definite local symptoms of sinus involvement except intranasal edema in both ethmoidal regions. The patient was in excellent general condition, but daily fever persisted, maximum 101 F. The sinusitis on the right side gradually subsided. February 4 transillumination showed a very cloudy left maxillary antrum and left frontal sinus. I made diagnostic puncture into the antrum under local anesthesia, using Hartman's method, and irrigation washed out gelatinous mucopus.

Taking into consideration the impracticability of intranasal surgery, and that the right sinuses had apparently healed spontaneously, thorough treatment was given a trial before resorting to the radical operation. Rest in bed, application of epinephrin-cocain on cotton, warm saline douches with moist heat dressings, literally steaming the face and frontal regions for hours daily, was tried. The pus flowed more freely and there was less fever, but there gradually developed local frontal and maxillary tenderness, with marked frontal and maxillary edema. Orbital edema was not a pronounced symptom. The radiograph by Mr. Dachtler confirmed the diagnosis of purulent sinusitis of the left maxillary and frontal sinuses. The right frontal was in doubt, but the slight cloudliness was probably due to the previous inflammatory infiltration which was subsiding. Dr. Lasalle saw the patient with Dr. Van Pelt and myself and concurred in advising operation to relieve the empyema of frontal, ethmoidal and maxillary sinuses.

The radiograph showed a rather large sphenoidal sinus immediately behind the ethmoids, but there was no way of determining whether or not it was purulent.

Operation.—February 9, in the seventh week of scarlatina, assisted by Drs. Lasalle and Van Pelt, Dr. C. E. Price anesthetist, at St. Vincent's Hospital, I operated by the Killian method, adapted to the acute suppurative condition. The maxillary sinus was explored through the canine fossa. It was full of pus. A large opening was made, the cavity curetted clean of abundant granulation tissue and a free opening for subsequent drainage made into the naris below the inferior turbinate. The sinus was then firmly packed to prevent bleeding into the throat during the operation on the upper sinuses.

The frontal sinus was entered by making a curved incision from the region of the trochlearis, following the orbital margin and downward nearly to the lower edge of the nasal bridge. The periosteum was separated and the floor of the frontal sinus exposed. The trochlearis was not disturbed. Pus flowed freely from the frontal sinus. The bone was eroded in the lower part, and there was granulation tissue in the infundibulum of this sinus. The radiograph gave us perfect surgical landmarks, size of the sinus, location of septum between the two frontals, and it was cleaned out from below without opening above the ridge. The septum was intact. The ethmoidal labyrinth was thoroughly curetted to the depth of two inches from the frontal prominence. On the radiograph, lateral exposure, the sphenoidal cell was two inches from the frontal margin, but I am not positive that it was entered as it is difficult to discriminate between the posterior ethmoidals and sphenoid.

Up to this stage of operation the nasal mucosa had been kept intact, the object being to keep blood and pus from flowing into the throat. The last step was to enlarge the frontonasal duct and establish a large free opening from frontal and ethmoidal sinuses into the nose. This was done without sacrificing the middle turbinate. There was no shock and but little pain following the operation. On the second day all gauze packing was removed, and all of the sinuses were thereafter daily irrigated with warm iodin solution. The canine opening was closed in about a week and irrigation was thereafter made through the large accessory opening beneath inferior turbinate.

The amount of pus in the daily irrigations gradually decreased and by the third dressing the temperature was normal. On the fifth day it rose to 102 F., with apparently favorable local conditions and no systemic cause determinable. This continued for several days reaching 103 F., and autogenous vaccine treatment was decided on. A culture from the ethmoid granulations was used by Dr. T. B. Cooley in preparation of vaccines. The streptococcus vaccine was sterilized and standardized, 1,000,000 bacteria to the minim. There was febrile reaction following the first five minims (5,000,000) but thereafter very slight if any. At intervals of three or four days injections to the total number of seven were given, gradually increasing the dose up to 10 minims. The result observed during the first week of this treatment was decidedly favorable. As the nasal mucosa became normally sensitive ½ per cent. phenol normal saline solution was used. In four weeks all pus discharge had ceased, and the frontal sinus opening was perfectly healed with an inconspicuous but slightly depressed scar. The frontonasal duct remained patulous, the opening into the ethmoid cells could be seen and the accessory opening into the maxillary sinus was still open. Six weeks from date of operation the patient was in normal health, hearing normal, and even the sense of smell was not impaired.

It is evident from a critical review of this case that it could not be classified as the most virulent type of streptococcus infection. It was characterized rather by extensive invasion. The general condition was favorable (no nephritis) and it should be added that the boy had the very best of nursing. This, combined with perfect hygienic conditions, was a factor in maintaining resistance. The temperature was not as high as would be expected in such extensive suppuration; in fact, there seemed to be an antifebrile toxic factor. The absence of severe cervical glandular infection was undoubtedly a factor in establishing a rapid and complete convalescence.

The question of serum or vaccine treatment of scarlatina is naturally introduced into this discussion. This disease is one that often taxes, I might better say, overtaxes, our therapeutic resources, and while the new treatment may be said to be in the experimental stage, yet there is sufficient encouragement to justify a thorough trial with the purpose of fortifying the system to resist the early toxic influences, and in the later stage to prevent the septic complications which are characteristic of this disease. The fact that this patient had had scarlet fever in infancy adds another complicating factor in the attempt to draw conclusions as to the merits of the vaccine therapy. Any treatment that will check suppuration in scarlatina will aid not only in preserving the function of organs involved, but also in preventing the spread of the disease, as it is a well-established fact that the discharges, and particularly nasal pus, is a carrier and disseminator of this contagium.

The advisability of the early use of autogenous vaccine treatment with the purpose of preventing sinus empyema in such a case as this is a subject for consideration. My own opinion is that the treatment was indicated early in the course of the disease—that is, prior to the development of empyema, with a possible chance of averting such an extensive operation. The second period of election was precisely as described—that is, soon after the operation, with perfect drainage established. Certain it is that convalescence was rapid and the sinuses were restored to normal in an unusually brief period, taking into consideration the extent of the empyema and that this boy had been sick in bed for nearly three months.

The early diagnosis of accessory sinus infection in the exanthemata deserves most careful attention and by timely treatment aided by vaccine therapy at the proper stage, and the radical operation if necessary, scarlatinal accessory sinus empyema may develop a surgical record comparable to that of the mastoid complications of this disease.

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STUDIES IN THE METABOLISM OF ATROPHIC INFANTS *

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The value of a food for an infant depends, in the broadest sense, on two factors: on the one hand, whether or not the food meets the requirements of the organism in furnishing sufficient energy and material for growth, and on the other, whether or not the food itself, or the substances derived from it in the process of digestion, exert any deleterious action on the organism.

Fundamentally associated with the first problem is the question of absorption of the food in the gastro-intestinal canal. In our system of infant feeding in which the percentage of protein, fat and carbohydrate in the food is the criterion by which we judge of its suitability, and by which we modify the mixture according to the clinical manifestations, it is important to know whether the absorption of the different substances is influenced by the percentage relation of one to another. Very few observations have been made on this point. The following studies on atrophic infants were undertaken with the purpose of determining the absorption of fat under the influence of different proportions of fat and carbohydrate, and the influence of the varying quantities of fat and carbohydrate on the nitrogen metabolism.

The methods used were as follows:

The infants were given a definite formula for periods of at least six days, and during the last three days of each period the urine and feces were completely collected. The fat and nitrogen content of the food was determined each day during the periods by analysis. As the carbohydrate excretion was not considered, the sugar intake was not accurately determined, but was computed from the average found in many previous analyses of milk, plus the amount of a 1 per cent. lactose solution added to bring the formula to the desired strength. As will be seen later, it was only necessary to know the approximate quantity of sugar, i. e., whether the sugar percentage was high or low. The urine was preserved by chloroform and kept on ice until the three-day specimen was completed. The total three-day specimen of feces was evaporated to dryness in the usual manner. By using a three-day period after giving the same formula from three to six days previously, the chances of error from irregular excretion,

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*From the William Pepper Clinical Laboratory, University of Pennsylvania.

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TABLE 1.—DATA CONCERNING EXPERIMENT IN CASE 1 TO DETERMINE FAT ABSORPTION

Date	Milk Formula	Fat, gm.	Sugar, gm.	Protein, gm.	Amt. each feeding ounces	No. of feedings	Beginning weight	End weight
			PERIOD I					
2/27 to 3/4	3.5—6.5 —2.5	135.	235.	83.	6	7	10 lbs. 9 oz.	10 lbs. 11 oz.
Stools yellow, soft, mushy; no curds.								
			PERIOD II					
3/4 to 3/10	3.2—1.75—2.	115.	68.	57.4	8	7	10 lbs. 11 oz.	10 lbs. 11 oz.
Stools yellow, formed; no curds.								
			PERIOD III					
3/10 to 3/16	1.2—6. —2.5	57.	80.	89.28	7	7	10 lbs. 11 oz.	10 lbs. 15 oz.
Stools yellow, fairly well formed; few small white curds.								
			PERIOD IV					
3/16 to 3/22	1.2—6. —2.5	57.	273.4	89.28	7	7	10 lbs. 15 oz.	11 lbs. 2 oz.
Stools semi-liquid, greenish, few rather large white curds.								

TABLE 2.—DATA CONCERNING EXPERIMENT IN CASE 2 TO DETERMINE FAT ABSORPTION

Date	Milk Formula	Fat, gm.	Sugar, gm.	Protein, gm.	Amt. each feeding ounces	No. of feedings	Beginning weight	End weight
			PERIOD I					
2/27 to 3/4	3. —6. —2.	141.	270.	76.5	7	7	11 lbs. 10 oz.	11 lbs. 14 oz.
Stools soft, liquid yellow; no curds.								
			PERIOD II					
3/4 to 3/11	3. —2. —2.	145.8	80.	67.1	7	7	11 lbs. 14 oz.	12 lbs. 3 oz.
Stools liquid, yellow; no curds.								
			PERIOD III					
3/11 to 3/16	1. —2. —2.5	57.	80.	89.28	7	7	12 lbs.	12 lbs. 1 oz.
Stools soft, semi-liquid, greenish-yellow.								
			PERIOD IV					
3/16 to 3/22	1. —6. —2.5	137.	273.56	89.28	7	7	12 lbs. 1 oz.	12 lbs. 6 oz.

as at times occurs in twenty-four-hour specimens, are largely eliminated. *It is to be especially noted that the figures throughout represent the combined total of three consecutive days and not the daily intake or excretion.*[1]

The histories of the cases studied and the notes of the different periods are as follows:

CASE REPORTS

CASE 1.—Albert H., white, aged 9 months, was admitted to the hospital early in January for acute bronchitis, which cleared in a few days; previous history of gastro-enteritis and malnutrition; bottle-fed (milk modifications unknown) since shortly after birth; father tuberculous and mother mentally deficient. On admission the child weighed 10 pounds, 7 ounces, and at the time of beginning the studies was nine months old and weighed 10 pounds, 8 ounces. During the intervening two months the weight remained almost stationary, although numerous milk modifications were tried. The stools were soft, greenish or yellow in color and contained occasional curds. Physical examination showed a child with flabby musculature and little adipose tissue; cannot sit alone; length 25 inches; circumference of head 16 inches; circumference of chest 15½ inches; circumference of abdomen 15 inches; anterior fontanelle open, measures 1¼x1½ inches; superficial lymph-nodes slightly palpable; slight beading of the ribs; heart and lungs negative; abdomen soft and not distended; reflexes normal.

CASE 2.—Edward, white, aged 10 months, was admitted to hospital January 8 for diarrhea and loss of weight, with a previous history of malnutrition with loose and offensive stools. The child was bottle fed after two months; had diphtheria at four months followed by discharging ear; family history negative. On admission he weighed 10 pounds, 10 ounces. Under treatment the ear condition improved and the stools became much better in character, being as a whole yellow in color and smooth, with only occasional curds. The weight curve was fluctuating and between the time of admission and the first period the net gain was only one pound; age at time of beginning studies (Feb. 27), 10 months; weight 11 pounds, 10 ounces. Physical examination showed slightly rachitic, atrophic infant, with flabby musculature. He could hold his head upright, but could not sit alone.

Circumference of head 17 inches, chest 15 inches, abdomen 16½ inches. Anterior fontanelle open—1 inch in width; heart and lungs negative; liver slightly enlarged; umbilical hernia; posterior cervical lymph-nodes enlarged; reflexes normal.

FAT ABSORPTION

The work that has been done on the absorption of fats in infants is a difficult subject to review and correlate. There are apparently many discrepancies in the results of the studies of fat metabolism that have been published, which we believe in the first place depend largely on the methods used. Kumagawa and Sutro[2] have recently studied this question, using known quantities of fat, and find considerable differences in the results obtained by several of the methods in common use. They have worked out a method which gives the most accurate results for total quantities of fat, but which does not permit of a separation of the fat in the feces into its component parts; i. e., neutral fats, fatty acids, and soaps. This is of considerable importance in the study of the feces in infancy, as it is supposed to bear an intimate relation to the question of the diseases of salt metabolism (rachitis, tetany, exudative diathesis, etc.). While the method we used gives results which probably vary from 5 to 10 per cent. from the total quantity of fat, the same error is carried throughout, and as the studies are comparative in nature this error is of little importance. It is also difficult to contrast the results of one worker with those of another, for although the studies as a whole are numerous, the conditions under which they have been undertaken differ considerably and the investigations are few in which any one point or question has been under consideration. A normal breast-fed or artificially-fed infant absorbs the larger part of the ingested fat. Bahrdt,[3] in the most recent and careful studies that have been made, using the Kumagawa method, finds an absorption of 93 per cent. in the normal child. A few years ago Freund[4] reviewed the various studies on fat absorption and from these and others since published it may be concluded that the normal absorption in a healthy infant lies between 90 and 95 per cent. The figures outside of these limits published as "normal" are probably due to either faulty methods or to disturbances in absorption. In both acute and chronic nutritional disturbances absorption of fats in the intestine is lowered, from 10 to 50 per cent. or more of the amount ingested being found in the stool. Practically all of this fat is derived directly from the food, a very small amount of ether-extractable substances being found in the stool with a fat-free diet. The loss of fat in nutritional disturbances is due to several factors, as altered digestion, accelerated peristalsis, admixture with mucus, etc. In our own cases the loss was from 15 to 33 per cent. of the quantity ingested. There is some question as to the form in which the fats are absorbed from the intestinal canal, but it is the generally accepted view that they must be split before absorption and are then recombined in the cells of the intestinal mucosa.

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[1] Fat in the milk was determined by the Leffman-Beam method and nitrogen by Kjeldahl. The nitrogen of the urine and of the feces was determined by the Kjeldahl method, and Ca by the method of McCrudden. In the fat extraction from the feces the method of Brugsch was used, which permits of a separation of the soaps from the neutral fats and fatty acids.

[2] Kumagawa and Sutro: Biochem. Ztschr., 1908, viii, 337.

Our problem, however, did not deal so much with the question of how much was absorbed, or the form in which it was absorbed, as with the question of the absorption of large and small quantities of fat, and the influences of varying quantities of carbohydrate on the absorption of the fat. The accompanying table (Table 3) summarizes our results as regards the first question.

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[3] Bahrdt: Jahrb. f. Kinderh., 1910, lxxi, 249.

[4] Freund: Ergebn. d. inner. Med. u. Kinderh., 1909, iii, 38.

TABLE 3.—SHOWING THE PERCENTAGE OF FAT LOSS IN THE TWO EXPERIMENTAL CASES DURING THE FOUR PERIODS

	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss Per cent.
Case 1—			
A Period I	135	20.08	14.9
Period IV	57	18.89	33.0
B Period II	115	21.21	18.0
Period III	57	14.05	24.6
Case 2—			
A′ Period I	141	23.18	16.5
Period IV	57	18.86	33.0
B′ Period II	145	29.53	20.2
Period III	57	18.95	33.0

When large quantities of fat are given the actual amount of fat in the stool is increased but the percentage absorption is much better. Average figures show this clearly.

	Per-Cent. of Fat in Mixture	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss, Per Cent.
Case 1	3+	125	20.65	16.0
	1	57	16.47	28.9
Case 2	3+	143	26.36	18.4
	1	57	18.90	33

In the 3 per cent. mixtures nearly five-sixths of the ingested fat was absorbed, while in the 1 per cent. mixtures a third was passed in the stool. Or, looking at it from another view-point, although there was about two and one-half times as much fat present in the food in the high fat periods, the feces contained only half again as much as in the low fat periods.

Somewhat similar results were obtained by Hecht[5] in a 12-months-old child in two three-day experiments:

	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss Per cent.
Period I	89.28	4.929	5.3
Period II	10.26	1.662	16.3

In this case, however, there was considerable stimulation of the intestinal mucosa when the low fat was given (Milchmalzsuppe made with Magermilch). During this period the child passed from five to six liquid stools daily and the two investigations may have different interpretations although similar in results. L. F. Meyer[6] likewise observed a difference in proportion between the fat intake and the loss in the feces (normal child):

	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss Per Cent.
1.	10.97	0.8	2.29
2.	35.95	1.588	4.44
3.	44.3	1.75	3.95

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[5] Hecht: Wien. klin. Wchnschr., 1907, xx, 497.

[6] Meyer, L. F.: Biochem. Ztschr., 1908, xii, 422.

Freund[4] gives a similar comparison between normal infants:

	Fat Ingested Daily, Gm.	Fat in Feces Gm.	Fat Loss, Per Cent.
Experiment 1—			
Period I	3.93	0.4468	14.27
Period II	16.50	2.4160	14.64
Experiment 2—			
Period I	3.17	0.5785	18.25
Period II	15.90	2.2590	14.21

In this case the fat loss in the feces bears the same percentage relation, with high and low fat intake. There are so many points of difference (age, method, time, etc.) between our observations and those of Freund that we do not wish to draw conclusions from a comparison between the two.

As fat and carbohydrate differ from protein, in that they may be substituted for one another within certain limits, as both are energy and heat producers rather than tissue builders, we combined high and low carbohydrate diets with the fats in order to determine whether the amount of carbohydrate exerted any influence on the absorption of fats. Thus in Table 3 in the periods grouped under A and A′ the food contained a high (6) percentage of sugar. In those grouped under B and B′ the food contained a relatively low (2 per cent.) amount. The total amounts are given in the accompanying Table 4.

Table 4.—High and Low Carbohydrate Diets Combined with Fats to Determine Influence of Carbohydrates on Fat Absorption

	Gm.		Gm.
Case 1—			
A Period I	235	B Period II	68
Period IV	273	Period III	80
Case 2—			
A′ Period I	270	B′ Period II	80
Period IV	273	Period III	80

Contrasting A with B, and A′ with B′ in Table 3, and considering the marked difference in the amount of carbohydrates in these periods, we are unable to find any apparent influence of the amount of carbohydrate on the absorption of the fat. Practically the same relation holds between the intake and absorption of large and small quantities of fat no matter whether a large or a small quantity of carbohydrate is present in the food.

As the quantity of nitrogen (see Table 6) in the food was nearly the same in all of the periods the explanation of these changes then must lie in the digestion of the fat itself. In no period was there a diarrhea present which might have accounted for the conditions. Moreover, the tolerance for or ability to absorb fat does not seem to be affected. In Case 1 there was an absolute absorption of 115 gm. of fat in Period I, while in Period IV the total quantity given was only 57 gm., of which a third (18.86 gm.), was found in the stool, only 1.2 gm. less than in the first period. A similar condition was present in Case 2. In none of the periods was the so-called "soap stool" of Czerny's "milk injury" or Finkelstein's "balance disturbances" present. We investigated, however, the question of soaps and calcium excretion and the results are shown in Table 5.

TABLE 5.—SHOWING DETERMINATION OF SOAPS AND CALCIUM

	Milk Formula	Fat in Stools Gm.	Soap Gm.	Soaps Per Cent.	Ca Gm.
Case 1—					
Period I	3.5—6—2.5	20.08	2.57	12.3	3.54
Period II	3.2—2—2.	21.21	2.00	9.4	2.51
Period III	1. —2—2.5	14.05	6.13	43.6	2.51
Period IV	1. —6—2.5	18.89	6.30	33.3	3.95
Case 2—					
Period I	3. —6—2.	23.18	3.58	15.2	3.54
Period II	3. —2—2.	29.53	2.29	7.4	4.21
Period III	1. —2—2.5	18.95	10.66	56.2	3.72
Period IV	1. —6—2.5	18.86	9.90	52.5	3.74

In both cases the absolute quantity of soaps was about three times more in the low fat periods than in the high, and the relative amount was increased on an average nearly five times. The amount of Ca excreted in the feces bears no relation to the absolute amount or relative proportion of soaps. If in these cases the infants were atrophic as a result of fat injury, the high fat periods should have shown the higher amounts and percentages of soaps. An explanation on these grounds, then, is wanting. Birk and Rothberg thought the formation of fat stools depends on the withdrawal of the earthy alkalies through their combination with fat, and they see in this withdrawal the cause of the failure to gain weight in this condition. Freund contends that the amount of soap formation depends on the reaction of the stool, which in turn depends on the bacterial changes producing fermentation when large amounts of sugar are present. A study of Table 5 shows that in Periods I and II, with a high and a low sugar intake, the soap formation was low, and that in periods III and IV, with a low and a high sugar intake, the amount of soap is high, averaging 48 per cent. (Case 1) and 54 per cent. (Case 2) of the total quantity of fat in the stools. Moreover, the amount of Ca in the feces does not bear any relation to the amount of soaps present, whether we compare it with the actual amounts of soap or the percentage relation to the total amount of fat.

We must conclude, then, that the changes are due to certain unexplained factors and that they do not support any of the above mentioned studies on fat metabolism in chronic nutritional disturbances.

NITROGEN METABOLISM

The second part of the study took up the question of the nitrogen metabolism under varying fat and carbohydrate percentages and in this we have confined ourselves to the nitrogen retention. It is a generally accepted fact that the amount of nitrogen in the feces is not proportionate to nor dependent on the amount of nitrogen in the food, although when increasing the food nitrogen from a very low or hungering period there is an increase of nitrogen in the feces. In investigations made by Kellar[7] on fasting infants an excretion of nitrogen in the feces of .0716 gm. and of .097 gm. in twenty-four hours was found after a preliminary period of thirty hours. In artificially fed infants the nitrogen amounts from 2 per cent. to 6 per cent. of the total weight of the dried feces.[8] Very little if any of the ingested nitrogen of the proteins is excreted as such although some of the nitrogen occurs in the form of their cleavage and putrefactive products. This together with the nitrogen of the gastro-intestinal juices and secretions, bacteria and epithelial cells, constitute the sources of the nitrogen of the feces. Although not directly dependent on the ingested food, it may be modified to some extent by the action of the food in stimulating or retarding the secretion of the gastro-intestinal juices, as the observations of Wohlgemuth and others have shown. It is very probable that, as in the case of Ca salts, the nitrogen absorbed may be excreted and reabsorbed in the intestinal canal. A glance at Table 6 shows no evident relation between the varying percentages of the food elements and the amount of nitrogen in the feces (i. e., nitrogen absorption). In Case 1 the amount varies from 1.345 gm. to 2.460 gm., while in Case 2 it is uniformly about 2.5 gm. in all four periods. For these reasons a study of the absorption is of little or no value and the important question is the study of the nitrogen retention. The nitrogen intake and the output in the urine and feces is shown in Table 6. The balance is considered as retained nitrogen, no account having been taken of the amount excreted through the skin. This is a small factor and in all probability would have been parallel throughout the periods in each case. So far as we know the only studies that have taken this into account are those of Rubner and Heubner,[9] and Tangl.[10] The former found a loss of 0.189 gm. of nitrogen per day in a normal child and 0.0338 gm. in an atrophic infant, while the latter found an excretion of 0.044 in an artificially-fed infant.

The nitrogen retention may be studied in two ways, either the total percentage retention (Nutzungswerth) or the retention per kilo of body weight. The figures for the latter (last column, Table 6) have been divided by three so as to give the retention per kilo per twenty-four hours, in order to compare our figures with those of previous studies. It will be noted that in all of our periods the retention of nitrogen was very good. The nitrogen intake in all of the periods was higher than was

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[7] Kellar: Arch. f. Kinderh., 1900, xxix, 123.

[8] Hecht: Die Feces des Säuglings, 1911, p. 24.

[9] Rubner and Heubner: Ztschr. f. Biol., 1899, xxxviii, 315.

[10] Tangl: Arch. f. d. ges. Physiol., Bonn (Pflüger), 1904, clv, 453.

TALE 6.—SHOWING NITROGEN INTAKE AND OUTPUT IN THE URINE AND FECES

Period	N in Food	N in Feces	N in Urine	N Retained	Per Cent. of N Retained	Retention per Kilo per 24 Hrs.
Case 1—						
I	13.460	1.345	5.080	7.035	52.2	.482
II	9.185	1.418	5.174	3.593	39.2	.246
III	14.285	1.968	7.812	5.505	38.8	.370
IV	14.285	2.460	6.506	5.239	36.6	.349
Case 2—						
I	12.243	2.144	4.340	5.759	47.0	.351
II	10.722	2.550	5.660	2.512	23.4	.152
III	14.285	2.438	6.930	4.917	34.4	.298
IV	14.286	2.610	4.700	6.975	48.8	.416

necessary for the development and replacement of the body tissues. Although it was our intention to have the nitrogen intake the same in all periods, the total amount by analysis was less in Period 2 in each case. In both of these periods the absolute retention is less although the percentage retention in Case 1 is practically the same as in Periods III and IV. It is evident that an increase of the nitrogen in itself leads to increased retention, but this opens a question which is outside of the scope of the paper. The highest percentage and best absolute retention is found in the high carbohydrate periods (I and IV). This is seen clearly in Case 2 in which the retention in the high periods averages 48 per cent. and 29 per cent. in the low. In Case 1 it is less marked as the difference between the averages is only 5.4 per cent., although Period I shows the highest percentage retention of all—over half of the ingested nitrogen being retained in the body. This is not due to insufficient calories in the food in the low carbohydrate periods, as between 75 and 80 calories per kilo were present in the food in Period III, which is the lowest period from the standpoint of calories. This observation is in accordance with those of Kellar and of Orgler. Orgler[11] studied the influence of lactose and saccharose on the nitrogen retention in a normal child and his results are summarized as follows:

Food	Food-N	Urine-N	Balance	Per Cent. Retained
300 gm. milk	1.7748	1.2853	+0.229	12.9
250 gm. malzsuppe	......	......	.....	....
10 gm. lactose	......	......	.....	....
10+50 gm. lactose	1.6743	.6824	+0.583	34.8
10+50 gm. saccharose	1.8272	.8369	+0.663	36.3

Kellar's[12] case is less conclusive, as the kind of food was completely changed, although the carbohydrates were markedly increased and the nitrogen remained practically the same:

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[11] Orgler: Jahrb. f. Kinderh., 1908, lvii, 383.

[12] Kellar: Malzsuppe, eine Nahrung für Magendarmkranke Säuglinge, Jena, 1908.

Food	Food-N	Urine-N	Balance	Per Cent. Retained
....	......	......	......	
½ milk c.mm. water	2.6725	2.0274	—0.2646	9.9
Malzsuppe	2.3443	1.4463	—0.417	17.8

As regards the quantity of fat in the food, we may simply state that as far as these observations show it is without apparent influence on the nitrogen retention. In comparing the nitrogen metabolism of the atrophic infants with that of healthy artificially-fed infants we find a paucity of studies suitable for such purposes as a result of the variations in body weight and in the kind and amounts of foods used. The best suited for this purpose may be taken from Hoobler's[13] study of a nine months' infant weighing about 8 kilos. Three periods of three days each with a high, medium and low fat percentage, with a nitrogen intake of 20.7 gm., 21.6 gm., and 25.5 gm., respectively, were studied.

The nitrogen retention per kilo of body weight per day was as follows:

Low fat	0.362
Medium fat	0.270
High fat	0.285

Hoobler found that about 33 per cent. was retained in each of the periods; in other words, the amount of fat was of little influence. He thought the retention of nitrogen was not influenced by the amount ingested—a conclusion we do not feel is justified by his studies. Hoobler does not give the percentage of carbohydrate in his milk mixtures, but it is probable that they contained about 6 per cent. as is customary in most of the milk mixtures in this country. Comparing our periods of high (6 per cent.) sugar with his we find a much higher percentage retention as well as a better absolute retention:

	Case 1	Case 2
Period I	.482	.351
Period IV	.349	.416

The better nitrogen retention of the atrophic infants may be due to their beginning on a period of convalescence, as both children started in to improve from the moment they were placed on the metabolic bed in the first period.

SUMMARY

In the study of these two cases of infantile atrophy—the results of which are similar—the following conditions were noted:

The fat absorption was less than in normal infants, although the infants were able to absorb large quantities of fat.

The percentage absorption was better with a large amount of fat in the food than with low amounts.

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13. Hoobler: Arch. Pediat., 1910, xxvii, 853.

The amount of carbohydrate in the food did not influence the fat absorption.

The amount of fat in the form of soaps in the feces was neither proportional to the amount of calcium in the feces nor to the amount of the carbohydrate in the food.

Both the actual and percentage amounts of soaps were greater when the fat intake was low.

The nitrogen retention was greater than in normal infants of the same age and weight.

Increasing the amount of the carbohydrate produced an increased nitrogen retention, but the nitrogen retention was not influenced by the amount of fat in the food.

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A PREPARATORY STUDY OF THE BACILLUS ACIDOPHILUS IN REGARD TO ITS POSSIBLE THERAPEUTIC USE *

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The recent advances in our knowledge of the biology of the gastroenteric tract have been so great that it seems time to begin a study of the practical use which can be made of individual organisms. Prominent among these organisms in the intestine is the obligate member of the acidoduric group, the *Bacillus acidophilus.*

It is to be noted in a general way that (1) this bacillus is a carbohydrate saprophyte; (2) it does not produce toxins; (3) it is a fermental organism, by fermental meaning an organism capable of breaking up the carbohydrates; (4) its habitat is the large intestine; (5) it thrives on carbohydrates, especially the sugars, such as dextrose, lactose and maltose; (6) it produces relatively large amounts of lactic acid from fermentable sugars; (7) it is antagonistic to the proteolytic organisms producing putrefaction, provided sugar is present; (8) although it produces acid it grows best when the medium is less acid; (9) it appears to grow better below the ileocecal valve than above; (10) it is of interest clinically because, under suitable conditions, when the host is placed on a carbohydrate diet, the organism becomes more abundant and it inhibits and even replaces to a considerable extent the bacteria characteristic of a protein regimen (this replacement of the protein flora by acidoduric bacteria is accompanied by the gradual diminution and even disappearance in the urine of those substances which are the products of protein decomposition in the intestine); (11) the *B. acidophilus* is non-pathogenic for experimental animals and under normal conditions is found to be an inhabitant of the intestinal tract of man; (12) it has the ability to render that portion of the intestine where it is localized unfavorable to the development of foreign invading bacteria, and (13) it can form a considerable amount of acid from carbohydrates, forming this acid mostly below the ileocecal valve.

In this same acidoduric group the *B. bulgaricus* has somewhat different characteristics. Its habitat is chiefly above the ileocecal valve, so that the acid which it produces must be transported to the large intestine and must act at a distance from the chief site of putrefaction and is, therefore, probably less effective than if it were generated at the seat of infection.

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*Read at the meeting of the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

Its action is most pronounced above the ileocecal valve and grows less as it approaches the anus and the bacilli are only sparsely found in the feces.

In contradistinction to the acidoduric group of intestinal bacteria are the proteolytic bacteria and their characteristics are suggestive of the antagonism which exists between the two groups. (1) The putrefactive (proteolytic) organisms attack and thrive on the protein elements of the food; in certain instances some may become invasive. (2) They may develop toxins. (3) The end products of protein break-down of certain of these organisms are found in the urine and appear as aromatic bodies, these bodies acting as evidence of proteolytic intestinal activity and in some measure acting as indices of such activity. (4) The habitat of this group is said to be chiefly in the large intestine and they are consequently more likely to be abundant below the ileocecal valve. (5) They flourish and increase best in an alkaline or neutral medium. (6) They are inhibited by an acid medium especially by the presence of lactic acid. (7) Certain of these proteolytic bacteria are facultative and as a rule when protein and carbohydrate substances are present they attack the latter first and spare the former. (8) The addition to the diet of easily fermentable carbohydrates, together with restriction of protein food is of material assistance in reducing the output of these putrefactive products. This results also in the diminution of the activity of the bacteria producing them.

There appears to be a considerable number of intestinal disturbances associated with the activities of putrefactive bacteria, some of which may be influenced by the activity of the *B. acidophilus.* As a well-known example of such putrefactive condition we might mention bacillary dysentery. There are three prominent bacilli which are associated with the clinical symptoms of bacillary dysentery: *B. coli,* streptococci and *B. dysenteriæ,* one or both types. So far, however, as the clinical picture of bacillary dysentery is concerned a differential diagnosis between these organisms cannot be made. The actual recognition of which of these organisms is producing the disturbance is dependent on the bacteriologic examination. Hitherto bacillary dysentery has been regarded as a disease brought about solely by the action of the dysentery bacillus. Now, however, it appears in most cases, at least, that the three organisms mentioned above working symbiotically in appropriate intestinal conditions produce the symptom-complex of bacillary dysentery.

It is to be noted here that in those instances in which the acidoduric group of organisms has produced lactic acid in considerable amount (through the influence of a carbohydrate diet), *B. coli,* in virtue of its being a facultative organism, changes its metabolism from the proteolytic to the fermentative type. In consequence of this change in metabolism from the putrefactive to the fermentative type, this organism (*B. coli*), which on the protein regimen produced putrefactive products inimical to the patient, and which was, therefore, a symbiote of the dysentery bacillus, now becomes an antagonist to it by forming lactic acid.

In like manner, although we do not know so much about the antagonistic action in this connection, it has been observed that the disturbing streptococci are lessened in number apparently by the action of the lactic acid. It has also been shown in regard to *B. dysenteriæ* that certain changes in its action are brought about by the influence of the change to the carbohydrate type of diet. These changes, so far as is at present known, are as follows: the bacillus, whether of the Shiga or Flexner variety, is normally of the proteolytic type, and, having gained entrance to the intestinal tract, locates itself chiefly below the ileocecal valve. It begins its attack on the protein in the intestine and produces toxins. The bacilli may penetrate the mucosa and even the tissues as far as the mesenteric lymph-nodes and thus establish the bacillus as an infectious organism. The toxins are absorbed and especially affect the anterior horns of the spinal cord.

It is evident that any beneficial therapeutic action on the infectious organisms, so far as the action of the acidoduric group on them is concerned, is to diminish their numbers and to prevent their production of toxins by rendering the medium in which they are growing unsuited for their continued development, thus reducing the amount of toxin which they produce. The damage brought about by the toxins already absorbed cannot be undone. Early inhibitory action of the acid-producing bacteria is therefore indicated.

It has been noted in the changes in flora which take place in the intestine, when by any means the putrefactive types of organisms are gradually changed to the fermentative type, that during the process the bacterial flora first returns practically to a normal type for the nursling, namely, to *B. bifidus* mostly, and to *B. acidophilus* to a degree. Then, as the carbohydrate of the diet is increased the acidophilus increases in number and greater amounts of lactic acid are produced. Care, however, must be taken not to allow the acidophilus to flourish to such an extent as to establish an acid intolerance in the host.

To be mentioned as of especial significance in an investigation of this kind are certain known possibilities in connection with influences which may be brought to bear on the intestinal flora, and changes which may be accomplished by varying the quality of the food presented to intestinal organisms.

The character of the intestinal flora of man, both with respect to the types of organisms represented, and to the nature of the resulting chemical activities, depends largely on the composition of the diet of the host. A moment's reflection will convince one of the accuracy of this statement; the intestinal bacteria, to a very considerable extent, derive their sustenance from the food in the alimentary canal, and as the food varies, so will the bacteria vary.

This variation in the nature of the bacteria comprising the intestinal flora can conceivably change in two distinct directions, following alternations in the host's diet: either the organisms representative, for example, of a protein regimen may be replaced by an entirely new flora when the host changes his diet to one potentially carbohydrate, or the bacteria characteristic of the protein flora can shift their metabolism to meet the new conditions established by the carbohydrate regimen. As a matter of fact, both possibilities are realized, so that we may recognize three distinct classes of bacteria when the food of the host varies from a protein to a carbohydrate diet. We recognize first an obligate proteolytic group of bacteria, which thrive on a protein regimen. These organisms, best exemplified by *B. putrificus,* are in reality to be regarded as bacteria characteristic of putrefactive conditions in the intestinal tract. They disappear largely when the food is changed to carbohydrate.

The second group, the obligate fermentative bacteria, grow best and are most numerous when carbohydrate forms a prominent part of the diet. These bacteria in virtue of the considerable amounts of lactic acid which they form under suitable conditions, are antagonistic to, and tend to replace, the obligate putrefactive (proteolytic) bacteria. *B. acidophilus* is the best known of this group. The third group, the facultative organisms, are those which accommodate, within limits, their metabolism now to a protein, now to a carbohydrate regimen. They are usually present in either class of food but are more numerous on the protein type of regimen, because they are less affected by the products of putrefaction, than those of fermentation. *B. coli* and *B. proteus* are perhaps the best known of the facultative group.

We recognize, then, three well-defined types of bacterial activity in the intestinal tract, the putrefactive or proteolytic type, acting on the protein, the fermentative type acting by preference on carbohydrate, and the facultative type, which is by far the largest and best known, acting either on protein or carbohydrate.[1]

It is interesting and particularly important to recognize that the intestinal bacteria of normal nurslings are strictly fermentative. This is what one would expect, because the diet of the nursling is one well suited to encourage a fermentative flora, being composed of over 6 per cent. lactose and only about 1.5 per cent. protein. The reaction of a normal nursling's feces, furthermore, is strongly acid, due to the formation of lactic acid within the intestinal tract by this fermentative flora. It will be seen later on that this lactic acid, formed by the activity of fermentative organisms, is an important feature in keeping down putrefaction. In this connection it should be stated that the flora of normal nurslings contains few, if any, putrefactive organisms. As the child grows older and is placed on a cow's-milk diet, a change takes place in the intestinal flora: this change occurs less rapidly if the diet is strictly limited to modified milk, more rapidly if the diet is made up of unmodified milk or with the addition of protein. The change consists essentially in the replacement of the characteristic fermentative flora of the breast-fed baby by greater or lesser numbers of putrefactive and facultative bacteria. It is marked by the beginning dominance of the facultative bacteria which tend to persist throughout life.

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[1] For a fuller discussion of these types, see Kendall, A. I. "Lactic Acid Bacteria: What They Are and What They Are Supposed to Do." Boston Med. and Surg. Jour., 1910, clxiii.

The cause underlying this change is not difficult to define: the change in flora is largely attributable to the relative decrease in carbohydrate, associated with the increase of protein, two conditions favoring the development of a putrefactive or facultative flora.

It may be accepted as proved that the fermentative flora of the normal nursling is a valuable factor in protecting the host from invasion by foreign organisms, particularly of the proteolytic type. Consequently the lack of such a flora is to be regarded as a weakness in the normal defence against bacterial invasion of the intestinal tract. It has been shown for example[2] that the intestinal flora in bacillary dysentery is essentially putrefactive in nature, at least in the more severe cases. It would appear logical and desirable, then, to attempt to reestablish and maintain the fermentative conditions at least in the intestinal tract of babies, and thus to encourage the reestablishment of the normal fermentative flora characteristic of such cases.

The question arises: How may this be accomplished? From what has been said it is evident that the increased administration of carbohydrate, and the restriction of protein will furnish the dietary conditions most favorable for the development of the appropriate organisms, and if the bacteria in question, the obligate fermentative bacteria, are present, and available in the intestinal canal, they may be brought up to their natural degree of activity. This process, however, takes a certain amount of time, and conditions may well arise in which the amount of time necessary to bring about this bacterial change will be prohibitive. For such cases, where time is a factor, and where it is desirable to populate the intestinal tract with useful types of fermentative organisms, the use of artificially prepared cultures of appropriate organisms is indicated, provided they can be obtained.

The observations presented in this paper are designed to show the feasibility of encouraging the growth of *B. acidophilus* by suitably modifying the food of the patient; if, however, acidophili are not present in the alimentary tracts of patients, it is apparent that they cannot be encouraged to grow even by the most careful dietary regulation. In such cases we deem it advisable, from the theoretical point of view, to introduce cultures of acidophili, provided they have been obtained from sources known to be normal and absolutely free from objectionable conditions.

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[2] Kendall, A. I.: Bacillary Dysentery, Boston Med. and Surg. Jour., 1911, clxiv, 288.

The characteristics of this organism (*B. acidophilus*) have been described fully in a previous communication[3] and need not be repeated here.

Cultures were readily obtained from two different patients by feeding maltose or lactose in moderate amounts. The details of the feeding experiments appear below.

The patients were first put on a diet in which protein was in moderate excess, and the characteristic protein flora dominated, as is shown by the protocols. As the diet was gradually changed to one in which carbohydrate predominated, there was a gradual restriction of the proteolytic flora, the more strictly proteolytic organisms diminished in numbers and the bacteria characteristic of the carbohydrate regimen, *B. bifidus* and *B. acidophilus,* gained the ascendency. These changes are of more than academic interest, for they indicate a possible method for controlling the proteolytic organisms, to a certain extent, at least, by dietary changes that are not only not harmful, but even under certain conditions beneficial to the host. While we are still quite in the dark concerning the absolute amount of importance to attribute to the presence of a more or less purely protein flora, the evidence is strongly in favor of the view that these organisms may not only be harmful themselves, but also that they may, and probably do, thrive in conditions suitable for the development of organisms like the typhoid or dysentery bacilli. On the other hand it is equally true that the conditions obtaining in the intestinal tract favorable for the continued development of the fermentative flora are inimical to the development of these pathogenic bacteria as well as for the putrefactive bacteria. Indeed, it appears to be a fact that the pathogenic organisms of the typhoid type, for example, are rather less resistant to the acids of the fermentative bacteria than are the more commonly met-with putrefactive bacteria which occur from time to time in the intestinal tract.

It is not a matter of indifference which fermentative bacteria are encouraged to develop in the intestines; furthermore, certain organisms appear to elect the small intestine, others the large intestine. As a well-known example of the former, *B. bulgaricus* may be mentioned, while *B. acidophilus* is found most plentifully in the large intestine. Applying these principles clinically, it would appear that putrefactive conditions in the small intestine might be controlled more readily by an organism that generated lactic acid in that portion of the alimentary canal, and *B. bulgaricus* would be selected for this purpose, while *B. acidophilus* theoretically, at least, would be more promising for putrefactions of the large intestine.

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[3] Kendall, A. I.: Jour. of Med. Research, 1910, N. S., xvii, 153.

We have shown that *B. acidophilus* was increased in numbers on the sugar diet, and this method of encouraging the growth of this organism would appear to be relatively simple. The time necessary to bring this increase in *B. acidophilus*, however, varies considerably and doubtless depends on the numbers and activity of the organisms of this type remaining when the carbohydrate regimen is instituted. There are cases in which it would be desirable, or even essential, to be able to introduce large numbers of acidophili with the minimal expenditure of time, and we believe that artificial cultures of this organism are indicated. The problem arises: Is it possible to cultivate *B. acidophilus* in artificial media and still have it retain its desirable properties? Further studies on this point are needed before the question can be definitely decided.

It is evident from what has been stated that it is worth while to investigate whether the inhibitory action of *B. acidophilus* on certain harmful proteolytic organisms can be made use of therapeutically, and it is with this object in view that we have done some preparatory work on this subject. The first step in an inquiry of this kind is to obtain a strain of the acidophilus which has been shown to fulfil certain requirements, just as has been seen done with *B. bulgaricus*. This strain should be kept in pure culture ready for use according to the physician's demand.

After a series of investigations our interests centered on the following two cases which seemed to well illustrate how we obtained vigorous specimens of the *B. acidophilus* by carrying out suitable modifications of the diet according to the principles which we have described. These cases illustrate, furthermore, in a striking manner the alternations in the types of the fecal bacteria following the changes in diet. It is to be noted in studying the bacterial changes in these cases that *B. acidophilus*, like other bacteria, is selective of the kind of sugar that it prefers and thrives on, and that it is apparently encouraged to a greater degree of activity in a medium containing dextrose or maltose than any other sugars.

CASE REPORTS

Case 1.—A boy, 6 months old, was being fed on a milk mixture containing a low protein, and for its sugar, lactose. The feces showed a moderate number of proteolytic organisms. On March 9 a high protein (3.50) was given and on March 13 the report of the feces was: Yellowish brown, with small curds; no mucus; slightly fetid odor. Bacteria: *B. coli*, *B. subtilis*, a few coccal forms; rather typical putrefactive feces both culturally and morphologically; practically no acidophili; many gelatin-liquefying forms. The food mixture was then changed to a low protein and the lactose replaced by a moderate amount of maltose—5 per cent. March 17 the report of the feces was: Yellow, with greenish color on the exposed parts; relatively homogeneous; odor not distinctive; *B. coli* and *B. subtilis* less in numbers; acidophili present in moderate numbers; a few bifid forms and a very small number of coccal forms appear; liquefying organisms greatly reduced in numbers and in activity. The maltose was then increased to 7 per cent. and the report on March 22 was: Yellow, granular and dry; *B. coli* and *B. subtilis* have almost disappeared; very few coccal forms persist; acidophilus and bifid forms increased. On March 27 the report was: Yellow, granular and relatively dry; bifid forms and acidophili present in considerable numbers; very few proteolytes; liquefying forms greatly diminished. On April 8 the report was: Small in amount, light color, with greenish color on exposed surfaces. Proteolytic bacteria have almost disappeared. Culturally, very few liquefying forms are left; they are very inactive; acidophilus and bifid forms still dominate.

In this case a markedly putrefactive intestinal flora was gradually changed to a practically normal nursling's, and then to one markedly acidoduric by providing at first a protein diet and then carbohydrate. The acidophili were vigorous and were separated and kept in pure culture. They were used to coagulate milk but did not make an entirely satisfactory buttermilk. The reason for this appears to have been that the culture obtained at this time was less vigorous than those usually obtained under suitable conditions. This is in line with the well-known variations which different strains of the same organism not infrequently exhibit in artificial media.

CASE 2.—A boy 17 months old, was being fed on a rather excessive protein diet and on March 13 a report of the feces was as follows: Greenish, homogeneous with a few small curds which were very hard; odor suggestive of putrefaction in intestinal tract (indol odor marked); culturally, *B. coli* few in numbers; many subtiloid organisms; a few coccal forms were present; liquefying forms numerous and active culturally; no acidophili found. The protein part of the diet was then decreased and on March 17 the report was: Light yellow, with slightly sour odor; good feces morphologically; *B. coli* still present in small numbers; *B. subtilis* present although in fewer numbers; liquefying colonies still active and numerous; practically no bifid forms or acidophili. The diet was then made largely carbohydrate and on March 22 the report was: Light brown, smooth, homogeneous; *B. coli* very few in numbers; *B. subtilis* greatly reduced, both numerically and in activity. Bifid forms appear in moderate numbers, together with acidophili; feces changing from the putrefactive to the fermentative type. On March 27 the report was: Brown, smooth, homogeneous; moderately voluminous; odor slightly sour; no starch demonstrable microscopically; culturally, very few *B. coli*, few *B. subtilis*, little liquefaction, and few liquefying forms; bifid forms in moderate numbers; considerable numbers of acidophilic bacteria; feces distinctly fermentative in type. On April 5 the report was: Smooth, brown, homogeneous; slightly acid reaction and sour odor; culturally, very few proteolytes were found and those that were recovered showed but little liquefying activity; bifid forms more numerous, acidophili dominant; typical fermentative feces.

In this case a markedly putrefactive intestinal condition was gradually changed under the influence of a carbohydrate regimen to a typical fermentative one. The acidophili were vigorous and were isolated and kept in pure culture. When introduced into milk the resulting lactic acid coagulation was exceedingly satisfactory and so this strain has been retained for further investigation.

Successive transfers must now be made with this strain of the acidophilus to see if it retains its useful properties of antagonism to the putrefactive conditions, which it has been shown to possess, or whether when used in milk it becomes acclimated and loses these properties. It is probable that it retains its strong lactic acid forming properties as does the *B. bulgaricus,* but if it does not it is possible that it may still be given therapeutically in a carbohydrate menstruum. If it can be given in this way it seems reasonable to suppose that the acidophilus will be superior to the bulgaricus in its power of inhibiting those putrefactive disturbances which are located below the ileocecal valve. It is here to be especially noted that while the activity of the bulgaricus grows less when it passes the ileocecal valve, that of the acidophilus increases, the latter always approaching in its downward descent its home, where it flourishes best, increases in number and vigor and produces most acid.

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ANAPHYLAXIS IN ITS RELATION TO PEDIATRICS *

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That anaphylaxis has an important bearing on many of the fundamental problems of medicine is indicated by the numerous recent laboratory studies both in this country and abroad. A satisfactory explanation of the phenomena would doubtless clear up a large number of diseases, and this is especially true of those occurring in early life. Questions of anaphylaxis and immunity are closely associated, and a better knowledge of the former would lead to progress in the latter.

Auer and Lewis have demonstrated that the immediate cause of death in sensitive guinea-pigs reacting to a second injection of antigen is asphyxia, due to tetanic contractions of the smooth muscles of the bronchioles, and that this contraction is probably peripheral rather than central in origin. Schultz has in a measure confirmed this view by showing that horse serum acting *in vitro* on excised smooth muscle fiber from a guinea-pig sensitized to horse-serum causes a contraction which is much more marked than when acting under the same conditions on the same tissues from a normal guinea-pig. While this action on the respiratory function is the most striking phenomenon of anaphylactic shock, there are a few other well-proved clinical symptoms. Pfeiffer claims that the most constant and delicate symptom of anaphylactic shock is a marked fall in temperature. That there is a fall in blood-pressure during the time of anaphylactic shock, both in guinea-pigs and dogs, has been repeatedly demonstrated. Biedl and Kraus, and Arthus have shown that another characteristic of the anaphylactic reaction is a decrease in the coagulability of the blood, while Michaelis, Fleishman, Slieswijk, Friedman, Friedberger, and Hartoch have demonstrated a measurable decrease in the complement content of the blood.

The symptoms, then, of the anaphylactic reaction are asphyxia, falling temperature, decreased coagulability of the blood, and an actual loss of complement. The heart continues to act for some time after the respirations have ceased.

While working on this problem and confirming some of the laboratory experiments, with a view to their clinical value, our attention was attracted by the marked parallelism of these anaphylactic symptoms and those described by Goodall, an eminent obstetrician and gynecologist of McGill University. He reported three cases of sudden death of infants which came under his observation. As he expresses the hope that his report of these cases "may draw forth evidence from other sources, either to corroborate or refute his conclusions," we shall use his material freely as a starting point for our discussion of anaphylaxis.

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Goodall's three cases were practically identical. The mothers suffered from a more or less severe postpartum eclampsia. The children, after their first "copious nursing," were seized with convulsions. The clinical picture is presented as follows: "Duskiness, cold extremities, blue nose, shallow, irregular respirations, and muscular rigidity from time to time in the lower extremities." Death in each case was due to respiratory failure; the heart continued to beat long after artificial respiration was instituted. There was no vomiting nor nausea. Emphasis is placed on the fact that these children were considered absolutely normal.

These cases are discussed by him with a view to answering the question whether an eclamptic mother should nurse her newly-born child. He asks: "Were these children healthy, and if not, what was the nature of their illness? Was there a toxin in the mother's milk which was fatal to them?" These are all questions which would naturally suggest themselves.

After reviewing the literature on the subject, he comes to the conclusion that many of the children born of eclamptic mothers have lesions of the kidneys, and therefore he considers that these apparently healthy children, to use his own words, "are far from being healthy." That he feels that this conclusion is inadequate is shown by the fact that he seeks another cause by affirming that the milk of an eclamptic mother is in itself toxic for her child. This toxin, he believes, is derived from the fetus and appendages. He attributes the eclampsia to the pregnancy, and the cure is the removal of the fetus with its appendages. Eclamptic attacks seldom, if ever, come on without uterine contractions having set in, resulting in pumping into the general circulation a large amount of toxins. It is these toxins, he concludes, which caused the death of these children, and this was the more easily brought about because the children were not as normal as they seemed.

We have given Goodall's explanation of the cause of death in these three cases in some detail, for the reason that they do and do not explain. The supposition of a possible kidney complication is not tenable, as the children were born healthy and remained so until after the first nursing. They showed no symptoms of kidney disease, and the convulsive seizures were not like those of nephritis.

That the mother's milk was in some way at fault seems certain. The attack came on shortly after the first "copious nursing," and clinically was the same as that in anaphylaxis. The symptoms were typical, and can easily be duplicated in the laboratory. The similarity to the symptoms of anaphylactic death is to be noted. The exitus was due directly to respiratory failure, the heart continuing to beat for a long time after the respiration ceased. There was also a fall in temperature. It would be interesting to know whether or not there was a fall in blood-pressure, but the only statement which in any way bears on this point is that the "pulse was slow and full."

Can the conditions as above outlined be duplicated in the lower animals? To bring about anaphylaxis in the lower animals, they must first be sensitized. The sensitizing agent is known as an antigen, and must be capable of causing the production of antibodies in the animal into which it is injected. In a general way these antigens belong to the group of either albumins or proteins. The reaction to this antigen is specific. For example, the same albumin or protein must be used for the second injection as was used to sensitize the animal. Rosenau and Anderson sensitized a series of guinea-pigs with guinea-pig placental extract, and after twenty-two days gave these sensitized guinea-pigs a second injection. Out of twelve guinea-pigs treated in this manner, eleven showed symptoms, and at least three had convulsions. These observations have since been confirmed by others. This series of experiments tends to show the possibility of sensitizing the mother with autolytic products of her own placenta. Goodall has specifically pointed out that eclampsia is always, or nearly always, preceded by uterine contractions, and these force into the general circulation the poisons which bring on the attack. Here we find all the conditions for an anaphylactic reaction duplicated. Uterine contractions, perhaps not noticed, have sensitized the mother; a continuation of the same process has forced into the general circulation a sufficient amount of the fetal products to bring about an anaphylactic reaction.

Can a child inherit its mother's sensitiveness to these toxins? Again, Rosenau and Anderson have proved that hypersusceptibility was transmitted through the female guinea-pig to her young; the male having no influence. This hypersusceptibility follows, whether the female guinea-pig is sensitized before or after conception, and is in no way dependent on the milk. These experiments prove conclusively that these children could have inherited susceptibility from their mothers.

Given the above conditions, the point still remains to be established as to whether or not it is possible to absorb a sufficient amount of unchanged protein or albumin through the gastro-intestinal tract to bring on a condition of anaphylactic shock. With a view to finding an answer to this question in our experimental work in anaphylaxis, four guinea-pigs were sensitized with whey, four with milk boiled two minutes, and five with untreated milk. Twenty-eight days later they all received 6 to 10 c.c. of milk mixed with carrots. All manifested at least mild symptoms, such as an increase in the rate of respiration and a desire to remain quiet in spite of disturbances which usually worried them considerably. Four out of the thirteen lay down on their sides. One of the number died.

In nine other sensitized pigs, diarrhea was artificially brought on by the administration of croton oil, after which they were fed with milk. The results were as follows: four very sick; rapid respiration; lie down and get up; one died of convulsions; four remaining pigs act sick, but no more so than the controls; refused to eat; four used as controls were very quiet; none had convulsions or died; none refused to eat carrots.

The above series of our experiments makes it clear that in guinea-pigs, at least, it is possible to bring on an anaphylactic shock by absorption of milk through the gastro-intestinal tract.

We were able to confirm Rosenau and Anderson's findings to a limited extent. regarding the possibility of sensitizing guinea-pigs with placental extracts. The placenta was ground up and allowed to autolyze at room temperature for an hour, and some of the resulting extract was injected into two female guinea-pigs. A second injection of 6 c.c. was given ten days later, with the result that one guinea-pig had a convulsion from which it recovered at the end of half an hour; while the other, for the same length of time, was very quiet, lying over on its side and breathing very rapidly.

It is our intention later to report on experiments in which we attempted passively to sensitize a series of guinea-pigs with a blood-serum from an eclamptic woman, and then note if at the end of twenty-four hours an anaphylactic shock can be brought on. The same experiments with milk alone would perhaps be as valuable, though less conclusive. It has been shown that it is possible to sensitize the mother with placental extract; that this hypersusceptibility may be transmitted to her young; and, finally, that a sensitized animal can absorb a sufficient amount of antigen through the gastro-intestinal tract to cause a condition of anaphylactic shock.

Does not this series of experiments show that Goodall's three infants died of anaphylaxis? Experimental facts and the clinical data are in perfect accord, and we feel that histologic examinations would have brought to light no pathologic conditions to explain adequately the symptoms exhibited in these three cases.

The factors which were so fatally important in these infants, probably in a somewhat less degree, have a bearing on many of the feeding problems of infancy and childhood—more especially in those in whom there is an idiosyncrasy to some especial form of food. Intolerance for egg-albumin, buckwheat, various fruits (as strawberries) and vegetables (as celery) are well-known examples. Many atrophic children fail entirely to digest cow's-milk, no matter what the modification, their only hope of recovery being in furnishing them with human-milk. These conditions, as a rule, begin in moderate digestive disturbances, and it seems fair to assume that a sufficient amount of unchanged milk-protein is absorbed to cause hypersusceptibility. It is well known that a quite constant concomitant symptom of this condition is a lowered body-temperature and a soft pulse. That these children do not rapidly die from convulsions or respiratory failure is due to the fact that there is a constant but small absorption of antigen. It is at the present time well recognized that an anaphylactic reaction may be entirely avoided or much decreased in severity by injecting into the general circulation minute quantities of the antigen before giving the second dose. The fact that these children so often recover when placed on human-milk, indirectly bears out this view. It is impossible to sensitize an animal with its own proteins; that is to say, a guinea-pig cannot be made hypersusceptible with the blood-serum of its own species. In the same way and for the same reason it would be impossible to cause an anaphylactic reaction in an infant with human-milk. If, on the other hand, milk from an animal of the same family is used, as for example a second injection of sheep's-milk into a guinea-pig sensitized with cow's-milk, we can obtain, in most cases, marked symptoms of an anaphylactic reaction. We should not expect, therefore, that a child who is doing poorly on cow's-milk would improve on milk from the same species of animal, while it might do very well for a time at least on milk from an ass. These observations suggest a difference in the protein matter of the milk of different species of animals. Of some importance also is the fact that infants quite regularly do well on almost any milk for the first week or ten days. Von Pirquet and Schick early in their studies on the so-called serum disease demonstrated the fact that there was an incubation period of from seven to nine days; and Rosenau and Anderson, in their work on horse-serum, found that guinea-pigs became susceptible to the second dose about the seventh or ninth day. This hypersusceptibility does not appear suddenly, but comes on somewhat gradually. Herein, perhaps, lies the explanation as to why it is that a milk mixture begins to disagree with a child at the end of about a week without any apparent cause.

While the recent studies in anaphylaxis have brought to light many facts which are at least suggestive in the field of infant feeding, there are other phenomena equally interesting when taken in connection with diseases common to children. Among these is the injection of animal serum into the human being for prophylactic or curative purposes. The sera which have been most commonly used are those which have been derived from the horse—as the antitoxin for diphtheria and, more recently, Flexner's serum in meningitis. These had not been long in use before certain clinical symptoms were noted; and occasionally even sudden collapse, with death in a few instances, resulted. The symptoms which followed the use of horse-serum are noteworthy in this connection, as in them are seen anaphylactic phenomena which in every way resemble those which can be produced artificially in animals. The study of this artificially produced anaphylaxis in human beings was first reported in detail by von Pirquet and Shick, and the symptoms of their so-called "serum disease" are given as urticaria, fever, edema and pains in the joints. As has been indicated, the symptoms in serum sickness are usually mild, but occasionally there is severe dyspnea, asthmatic in type, and, rarely, sudden death. The first and best known of these tragic cases is that described by Langerhans.

> "A child 1½ years old, received 2 c.c. of antitoxin subcutaneously. Before the injection the child was cheerful, but five minutes later he became restless, cried, and then began to have great difficulty in breathing. The skin over the whole body became cyanotic; finally there was a severe convulsion, the pupils becoming widely dilated, and foam appeared at the mouth. Seven minutes after the injection, the child was dead."

A number of such cases have been reported in the literature. The symptoms are always identical, and frequently the statement is made that the heart continues to beat long after respiration has ceased. While these instances of sudden death are intensely interesting, the symptoms of the milder types of the disease are still more so, as *they suggest an etiologic factor for a number of clinical conditions which at the present time are far from being clear.*

It has long been recognized that urticaria is closely associated with certain food idiosyncrasies, and that all types of the disease yield quickly to dietetic measures. It has been classed with eczema and angioneurotic edema as a form of "exudative diathesis." These diseases bear a marked resemblance to conditions which are occasionally associated with a second injection of antitoxin in children. While it has not yet been possible to produce experimentally skin lesions analogous to eczema, it is suggestive that therapeutically the disease is best treated by a radical change in diet, with especial care to increase the functional capacity of the eliminative organs. In any event, it would not be expected that experimental proof would be conclusive, as in a condition so chronic it would be necessary to carry on the work over a long period of time, which of itself would preclude obtaining any definite results in children.

Localized reactions to a second injection of antigen occur best in those animals which give the more generalized phenomena with the greatest difficulty. The only animal which regularly gives the general symptoms of irritation, paresis and respiratory failure is the guinea-pig. These generalized symptoms can, however, under proper conditions, be produced in all animals, including man, as has already been pointed out. This observation is an important one since it serves as an explanation of certain localized diseases. Arthus first noticed necrosis at the point of injection in rabbits. Lucas and Gay, some time later, made the same observation on human beings. Elliotson, as far back as 1831, traced the cause of hay fever to certain kinds of pollen, and Blackley and Dunbar have rather recently confirmed this observation. They were able to produce this disease at will, even in the winter, by exposing individuals subject to hay fever to small amounts of pollen, whereas normal individuals do not react in the least under similar conditions. This reaction is not due primarily to an endotoxin, as Wolff-Eisner has suggested, but is a true, localized anaphylactic reaction. That this is not a constitutnoial idiosyncrasy is shown by the fact that children do not suffer from hay fever, the first attack appearing some time between the tenth and the twentieth years. However, some of the forms of asthmatic bronchitis show a type of reaction similar to that of hay fever.

Freiberger describes the case of a young man who was highly susceptible to horse-albumin. He could go about among cattle without developing any symptoms whatever, but as soon as he came near a horse he would be seized with asthma and have severe respiratory disturbances. This hypersusceptibility was so great that it was necessary for him to ride in the back seat of a wagon, and even then he did not always escape an attack. That these attacks were due to emanations from the horse was shown by the fact that he was much less liable to them if the horse had been recently groomed. It subsequently became necessary to give this young man a prophylactic injection of 2 c.c. of antitoxin (horse-serum). Five minutes after the injection he was seized with an attack of difficult breathing, and within ten minutes had developed a severe asthma. With this there was falling temperature and great prostration. In short, he had a classic anaphylactic reaction. In one hour he was much better, and in two hours he had entirely recovered. The sequel was highly interesting, as during the three months following he was immune to horse emanations, as was repeatedly proved experimentally. The cure, however, was not permanent.

Wiley cites a case in which there was this same hypersusceptibility to horse emanations, in which a dose of 2 c.c. of antitoxin (horse-serum) resulted in prompt death.

Asthmatic attacks in every way analogous to those just cited are not uncommon in children, and are not infrequently confounded at first with pneumonia. The children who are subject to these attacks have them, as a rule, at frequent intervals, sometimes as often as once or twice a month. The Germans, following Finkelstein's classification, consider laryngeal spasm, tetany and eclampsia as part of the "spasmophile diathesis," and, more recently, one of us (Pisek) suggested in a monograph that all those conditions which were marked by spasm of some portion of the respiratory tract—as asthma, for example—be included in this classification. It is, of course, to be understood that this group does not include, at least specifically, those cases in which an actual physical anomaly is present. These spasmophilic conditions have long been regarded as the result, directly or indirectly, of exaggerated irritability on the part of the child's nervous system. They are most often found in children who have suffered from disturbed chronic metabolic processes during the period of growth and development.

One of us (Pisek) recently had under observation an infant suffering from tetany in which the attack could be brought on almost at will by feeding the infant with whole milk. This child presented evidences of rickets and symptoms of intestinal indigestion. Later it did very well on a whey-cream mixture, but it was three months before untreated milk could be added to its dietary without causing marked symptoms of tetany to appear. Perhaps symptoms which we have long considered as due to unstable nervous equilibrium are in reality mild forms of anaphylactic reaction. The suddenness of onset and rapidity with which they disappear would certainly suggest it. It is certain that they occur under circumstances which most favor absorption of unchanged or slightly changed proteins from the intestinal tract, for we have already shown that an irritated gastro-intestinal tract is most favorable for absorption of antigen in sensitized guinea-pigs. Under these circumstances death would not ordinarily occur for the reason that the antigen would be absorbed only in minute quantities, which of itself would tend either to do away entirely with the attack or, if the amount were slightly larger, to produce mild symptoms.

In this connection it is not unreasonable to suggest that some of the severer types of convulsive seizures may be anaphylactic in origin. It is recognized that previously healthy children attacked with acute infectious gastro-enteritis rarely have convulsions at the outset. A study of our clinical cases is evidence that children who have suffered from a mild and insignificant digestive disturbance for some time are most apt to be seized with a convulsion when the intestinal disturbance becomes exacerbated.

Rist, Axamit, Rosenau and Anderson, Kraus, Doerr and Freiberger have all shown that bacterial proteins are capable of causing the anaphylactic reaction in guinea-pigs. Freiberger and Goldschmid found that by leaving the bacteria in contact with the amboceptor (specific), then later carefully washing and finally mixing them with fresh guinea-pig serum, after a while a poison was produced which in doses of 2 to 4 c.c. quickly caused the death of guinea-pigs with all the symptoms of anaphylaxis. It would seem from these findings, paradoxical as they appear, that these reactions are merely quantitative differences in the same curative processes. We must, therefore, regard both of these factors in our consideration of infectious diseases. With the invasion of bacteria the formation of antibodies begins, and as these antibodies are formed there is an anaphylactic reaction taking place. The formation of the resulting poison or anaphylactin is at first so small in quantity as not to cause immediate death. At this point another interesting factor enters. Vaughan has shown that anaphylactic reactions may be prevented in whole or in part in a sensitive guinea-pig by preceding the second dose with a very small quantity of the antigen. As the production of anaphylactin in the earlier stages of an infection is very minute, the constant tendency is to diminish the severity of the anaphylactic reaction. As an example let us consider a sickness with a crisis, as pneumonia. If, on the one hand, the production of antibodies takes place rapidly enough to destroy all the bacteria, and, on the other hand, the number of bacteria are insufficient to form a toxic dose, then there follows a critical healing. On the contrary, if the amount of strange protein is so great as to cause the formation of a toxic dose, exitus follows. Again, if the amount of antibody formed is small, then the destruction of bacteria will be so minute as to cause a mild grade of anaphylactic reaction, and then we will have the clinical picture of a protracted course. The temperature-curve in a pneumonic crisis is quite typical, often falling to or below normal in a comparatively short space of time. *This is in accord with anaphylactic phenomena.*

The conditions as described in pneumonia hold good in these exanthemata, in which there is an incubation period of seven to ten days, the organism being flooded with parasite albumin, and the final critical formation of anaphylactoxins, with the appearance of the antibodies. The course of the exanthemata runs a close parallel to the serum disease, and the analogy between these diseases and vaccination for small-pox is certainly close, as von Pirquet pointedly put in his work on "Serum Krankheit."

Special reference may also be made here to the nephritis which follows scarlet fever. It is quite apt to appear at about the third week of the illness, and may be looked on as a sort of relapse. The explanation lies in the probability that the formation of antibody was not sufficient to destroy all the bacteria, and with their growth in numbers a sufficient amount of anaphylactoxin is produced to cause a relapse which is local and not general in character. This assumption is borne out by the observations of Shick, who noticed that during the third week other symptoms, such as lymphadenitis, characteristic rise of temperature, and occasional relapse all occurred at about this time and only at this time. This very process occurs in tuberculosis and typhoid. Thus it is seen that we have, on the one side, the bacterial albumin, and on the other the formation of antibodies and the partial destruction of the bacteria, with a more or less active anti-anaphylaxis, in this way accounting for relapses or a protracted course.

It has been our effort to correlate some of the many isolated facts which have come from the laboratory, and to attempt to bring them into intimate relation with clinical pediatrics. Through such experiments a clearer conception of the fundamental problem of disease has been obtained, and should lead to improved methods of prophylactic and curative treatment. In the theories advanced, perhaps, will be found the explanation of some of our empirical treatment, and it is hoped that this contribution will suggest new lines of treatment and stimulate other clinical workers to gather evidence in this branch of medical science.

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THE FUNDAMENTAL REQUIREMENTS OF AN INFANT'S NUTRITION *

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The requirements for an adult's nutrition under the most varying circumstances are definitely known. The amount of food that is necessary to keep him in a state of equilibrium when at rest, when exercising moderately and when undergoing the most violent exertions, has been determined with scientific accuracy. These determinations may be repeated as often as wished, and, provided they are properly made, will give uniform results. They are laborious and time-consuming, but yield trustworthy data because, with the assent and the cooperation of the adult subject, the conditions can be absolutely controlled.

It is not so with children or infants. There is no reason to believe that in them the laws of nutrition differ in any marked way from those of the adult, but the control of conditions so as to make our results trustworthy is extremely difficult, and we are able to obtain, at best, only a part of the information that we wish, accurate though this be. I shall speak of this more fully later, because it is the one, and apparently the only, insurmountable obstacle in the way of the most scientific and satisfactory accuracy in determining the food requirements of the infant.

There are certain fundamental facts that must be considered in dealing with this subject. The warm blooded animal requires energy for the life processes of the organism, the heart-beat and circulation, the respiration and the activity of the various organs and glands, and the heat produced by these processes, with the assistance of the physical vasomotor control, maintains the cells at their normal tropical temperature. in which they functionate to the best advantage. Energy is also required in addition for the animal's endless muscular activities. The energy that the body expends is all given off and may be measured as heat—all except that energy contained in substances in the urine and feces that have failed of complete combustion and which for the present may be disregarded. It is therefore quite logical to speak of the energy expended in terms of heat-units and of the food that is ingested to furnish this energy and which is readily converted into it, in the same terms.

If the output is known, the human body may be retained in a state of equilibrium by furnishing an amount of energy in the form of food

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equal to this, and, as I have said, the output is, especially in adults, capable of being measured. It is obviously impossible to do this for each patient that must be fed, but Rubner's work makes this no longer necessary. Pettenkofer and Voit measured the output of different men under the same conditions, but were unable to decide what it was that determined the varying amount of energy loss. It was Rubner's great service to point out that the heat production and dissipation, or, in other words, the amount of energy lost, are, under similar circumstances, proportional to the surface area of the body. This law enjoys the widest applicability. The lion and the mouse, the infant, the grown man and the giant give off the same amount of heat per square meter of body surface, provided the conditions are the same. The importance of the skin surface is thus apparent.

An accurate method for the determination of the body's surface area is, therefore, necessary. The formula usually employed is

$$\sqrt[3]{\text{Wt. in gm.}^2}$$

multiplied by a constant, 12.3 or 11.9. For the average well-nourished child or adult, this formula gives excellent results. It is not, I believe, from the results of some of our experiments, accurate for poorly nourished or emaciated beings, and a formula which will give information as to the surface area of these is desirable and capable of being constructed.

We are further indebted to Rubner for determining by a series of thorough and painstaking experiments the utilization of the various foodstuffs and the amount of energy that each is capable of furnishing to the body under normal conditions of digestion, assimilation and excretion. Fat furnishes to the body 9.3 calories of energy per gram ingested, sugar 4.1 and protein 4.1, without reference to the products of incomplete combustion that are eliminated in the urine and feces. The saving of labor as a result of these determinations has been immeasurable, and it is because of these determinations that we may disregard the elimination of the products of incomplete combustion in the urine and feces.

In order to determine the food requirements of an infant, we begin with the assumption that the energy required to keep him in a state of equilibrium is equal to his output. If then, we measure accurately his output, we know definitely the amount of energy required to keep him in equilibrium. To this must be added the amount of energy necessary for his growth. But in order to measure the output, the conditions must be always the same and with the child the conditions can be the same only during sleep. Nothing alters the metabolism so much as mechanical work, and when awake the infant is always performing this, and the amount that each one performs is by no means the same and cannot well be estimated, though in the individual case it may be experimentally measured.

Rubner and Heubner dispose of the necessity for keeping the conditions always the same by saying that an infant cannot perform a very measurable amount of work, and that whether he is awake or asleep will not greatly alter the results. Their determinations were always made over prolonged periods, twenty hours out of the twenty-four, with the child sometimes awake, active and crying, and sometimes asleep. Schlossmann's results were obtained in much the same way.

During the last year in Dr. Lusk's laboratory, we made experiments with different children with a calorimeter of the Atwater-Rosa-Benedict type, especially constructed for use with small children and animals, which allows a determination of the heat produced, as well as of the oxygen consumed and the CO_2 excreted, with an error of less than 1 per cent. We could show, first, that it is possible to use for comparison only sleeping hours, and that the increase in metabolism in the waking hours is very great over that in the sleeping. For instance, one boy, J. E. N., who produced during sleep 961 calories per square meter of body surface, calculated for twenty-four hours, produced 1,065 calories, similarly calculated, when awake, and 1,130 calories when crying; and another, W. McG., 1,092 calories when asleep, 1,264 when awake, and 1,514 when vigorously crying.[1] Schlossmann has also shown by determinations of the respiratory exchange on the same infant when asleep and when crying, that the metabolism could be nearly doubled, and that an infant weighing only 5 kilograms, when vigorously crying, expended one-fifth as much energy as a full-grown man at hard labor.

It is obvious, then, that children can be investigated satisfactorily only during sleep. This is unfortunate. It makes the one weak link in the whole chain. We can measure exactly how much energy is given off, and consequently how much is required, during the absolutely quiet hours, but the extra amount necessary for muscular exertion remains undetermined.

We made many experiments on a healthy well-nourished child 3 months of age, weighing 4.75 kilos, or a little over 10 pounds. He was fed every four hours during the twenty-four, so as to keep his metabolism as uniform as possible. He was put in the calorimeter shortly after a feeding, and his metabolism determined during a period of three hours, but only sleeping hours were used for the averages. It was found that he produced heat which, calculated in the ordinary way per square meter of body surface for twenty-four hours, was equal to 952 calories.[2] I think it would be safe to say that the requirements for an infant completely quiet would be not very far from this, and that from 940 to 975 calories per square meter a day would allow sufficient latitude.

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[1] The difference in the calculated metabolism of these two children when sleeping I believe to be due to the fact that the formula employed for calculating the surface area does not give correct results with poorly nourished children. The second child though lighter than the first was 3.5 cm. longer. Too small a calculated surface area gives too high a metabolism per square meter of surface.

There are no figures with which these may be compared, as the heat produced by children has never before been directly measured; nor have the sleeping usually been separated from the waking hours, as it had not seemed sufficiently important to do so. Rubner's and Heubner's determinations were made, as I have said, over twenty hours in the twenty-four, the children being awake part of the time. It was impossible to continue the experiments throughout the whole twenty-four hours on account of the feeding, and as the most active periods were those shortly before and after feeding and during the bath, much of the effect of the activity was lost. It cannot, therefore, be considered that their twenty hours represent accurately an average of the twenty-four.

Their determinations on different children were 1,054, 973, 1,106 and 1,180 calories per square meter per twenty-four hours.[3] The increase over the figures which we obtained is undoubtedly to be accounted for by the mechanical work that their children performed while awake. The highest figures that they ever obtained, 1,180, were with a very active child who cried much of the time.

If we consider that 940 to 975 calories per square meter of body surface in twenty-four hours is the requisite in sleep, we can only estimate the extra amount required by muscular exertion, and this estimation is extremely difficult, and any errors likely to be enormous. One child differs so much from another in all of his habits; the first may sleep twenty hours out of the twenty-four and be peaceful, quiet and lethargic, seldom crying, and lying contentedly still; the second may sleep only fourteen or fifteen hours, and when awake may be constantly in motion, crying, struggling, turning and twisting, and in all of these extra hours he demands more energy which, as may be seen from the figures that I have quoted, may exceed the energy-demand in the sleeping hours by 40 per cent. or more.

I have reiterated this in order to emphasize just where the difficulty lies. We know the resting requirements, and we know sufficiently accurately the requirements of growth. Cammerer, by the statistical method, which determines the total food intake and urinary and fecal output, showed that one breast-fed infant retained 15 per cent. of the energy-content of his food for growth, and another, 9 per cent. Rubner and Heubner determined that an artificially-fed child retained 12 per cent. for growth. There is apparently a fixed and definite tendency toward uniform growth, and a definite proportion of food is retained for this purpose. Growth is the natural tendency of the child, and energy sufficient for this must be supplied in order to keep him in a normal condition. It appears that 10 to 15 per cent. in excess of the energy required for equilibrium maintenance makes ample provision for growth.

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[2] I have used 12.3 as the factor in determining the surface area.

[3] Rubner and Heubner used 11.9 as the factor in determining the surface area. I have recalculated their figures, using 12.3.

The requirements for growth are thus seen to be relatively small and by no means explain the great difference in the nutritional demands between the infant and the adult, although before the days of exact measurements this was supposed to be the only reason why the young infant required 100 calories, and the adult 35, per kilogram of body weight. Rubner gave the true explanation, that the difference was due to the relatively greater surface area. The smaller the body, the greater the surface area in comparison with another body of similar composition. As the smaller body increases in size, its surface area becomes relatively less and less, and it is for this reason that the requirements of normal children shrink from approximately 100 calories per kilo in the first few weeks of life, to about 70 per kilo at the end of the first year, and not because the rapidity of growth has undergone any great diminution.

There are known, then, the resting requirements of the infant and the extra quantity necessary for growth, but that amount over and above the other that is necessary to compensate for the activities of the waking hours, is as yet to be obtained only by estimation.

I have refrained from approaching my topic from the side of practical application because, at the present time, it does not seem that we are in a position to utilize the results of the determinations that I have spoken of in an entirely satisfactory way. There are still some additional data that must be supplied, but that it will be possible to do this at some future time I feel reasonably sure.

But the requirements of an infant's nutrition refer to quality as well as quantity. Water must be furnished to the infant in large amount compared with the adult, on account of the infant's great cellular activity. His smaller mass of cells is called on to do almost three times the work that those of the adult have to perform, and they do this to the best advantage only when water is freely provided them.

The salts of potash, sodium, magnesium and calcium are all vitally necessary for the life processes. They are all present in the proper proportion in woman's milk, and are sufficiently represented in any dilution of cow's milk that would be used for any considerable length of time. In the majority of instances, they are in excess in the dilutions given to children, but this excess is not a factor of importance with the healthy child, which is the one that is under consideration. The salts of iron are, however, deficient both in human and, especially, in cow's milk. The large supply of iron present in the liver and other organs of the newly-born, may gradually be drawn on, and evidently is intended to be drawn on, during the first year, but this deficiency of iron is one important reason why an exclusively milk diet should not be persisted in too long.

The fats and the sugars are the great providers of energy, and together they furnish approximately 90 per cent. of the body's requirements. To a large extent they may be used interchangeably, and an excess of one may for a time compensate for the deficiency of the other, though not indefinitely. Whatever disturbances these produce, are chiefly recognized by gastro-intestinal symptoms such as vomiting, diarrhea, or soapy stools, and so forth. A deleterious effect of either of these on metabolism, so far as the exchange of energy is concerned, has not been demonstrated.

With the protein it is different. This must be furnished in a digestible and assimilable form to repair the loss by wear and tear and to provide for growth, but beyond a certain point there is a marked disadvantage in giving protein. This is not because the casein of milk is difficult of digestion, but because of the effect on metabolism known as the specific dynamic action of protein. By this action, the total heat production of the person ingesting the protein is raised, often to a marked degree. This increased heat must be disposed of. It may be available for warming the body in cold weather, but is an added source of discomfort and possible danger in hot weather, when it is difficult to get rid of sufficient heat by radiation; and it may cause a dangerous elevation of the infant's temperature when the heat-regulating mechanism is not fully developed. In addition, the extra ingestion of protein throws additional work on the organs of digestion, and the processes of intermediary metabolism.

Two experiments that I have made indicate this very well. One child, who produced an average of 952 calories per square meter in twenty-four hours, was given, in addition to his regular diet, 15 gm. of nutrose during the twenty-four hours. Nutrose contains nearly 90 per cent. of protein. As a result of this extra protein his heat production rose to an average of 1,051 calories per square meter, or a little over 10 per cent. The metabolism of another child rose from 1,097 to 1,383, or an increase of 26 per cent., with the addition of 30 gm. of nutrose. This represents an undue, unnecessary and, at times, undoubtedly harmful tax on the organism.

It is probable that slightly less protein is required for maintenance and growth in breast-feeding than in cow's milk feeding, owing to the better utilization that can be made of the homologous protein, but the excess required with cow's milk feeding is undoubtedly slight. When feeding a normal child, protein should furnish not less than 8 per cent. and not much more than 10 per cent. of the total energy in the food. When it furnishes 15 per cent., the specific dynamic action becomes noticeable, and when it furnishes 20 per cent., the effect is very marked.

It will be seen, therefore, that in addition to the quantity of the food provided, a proper disposition of the energy among the various constituents is always seriously to be kept in mind.

PROGRESS IN PEDIATRICS

NOTICE

Circular issued by the American Orthopedic Association and the American Pediatric Society in reference to acute epidemic poliomyelitis, addressed to health authorities and boards of health.

Anterior poliomyelitis is, so far as known, a communicable disease, being communicated from one patient to another and also by means of a third person. It occurs in epidemics and tends to spread along the lines of greatest travel. There is reason to believe that it is prevented from spreading by quarantine, and with the very great prevalence of the disease in the summer of 1910 it is the opinion of this committee that it is essential that it should be made a reportable disease in all states in order that its presence may be detected and its spread guarded against.

Of particular significance are the so-called abortive cases, in which indefinite ailments occur in children in communities where frank paralysis also exists. These abortive cases of infantile paralysis are undoubtedly a source of infection, and their record and study is of much importance. In a community where cases of infantile paralysis occur, cases of illness with sudden onset of fever and meningeal symptoms should be closely watched and regarded as possibly infectious. In such cases even recovery without paralysis does not establish the fact that the case was not abortive infantile paralysis.

All cases of infantile paralysis should be strictly quarantined, sputum, urine and feces being disinfected, and the same rigid precautions should be adopted as in scarlet fever. This quarantine should, in the opinion of the committee, last for four weeks, in the absence of definite knowledge as to when the infection ends. Children from infected families should not be allowed to go to school until the quarantine is abandoned. The transportation or transfer of acute cases in public conveyances should be strictly forbidden. It would be very desirable to adopt provisional quarantine measures in suspicious cases in a community in which an epidemic prevails.

The report of all cases of infantile paralysis to the public health authorities should be enforced by law, and all deaths from this cause should be properly described and registered. A careful study of epidemics by public health authorities is strongly advised.

Robert W. Lovett, M.D., Chairman.
Henry Koplik, M.D.
H. Winnett Orr, M.D.
Irving M. Snow, M.D., Secretary.

ANATOMY, PHYSIOLOGY AND HYGIENE

School Inspection in Small Towns

(*Arthur Tracy Cabot: Boston Med. and Surg. Jour., 1911, clxiv, 633*)

Cabot advances the proposition that the best school inspection and supervision in towns and small communities is obtainable by a nurse alone. He cites the experience of two years in Canton where the method has been tried with perfect satisfaction. Inspection by a competent physician is expensive and is very difficult to obtain, because in small places the physician's close supervision of the children is interfered with by the professional jealousy of the other physicians. The nurse in Canton looks after 900 children. She examines them at the beginning of the year and records the results in a card catalogue. She keeps a record of any illnesses they may have during the year. Children showing any infirmity of eye, ears, throat or general condition are referred to their physicians and followed up to see that they get advice and follow it. The nurse also gives talks on matters of hygiene. This teaching is reenforced by visits to the homes. Arrangements have been made with the dentists of the town to treat the poor children on certain afternoons at half price. The contagious disease problem is easily handled by the nurse working in conjunction with the board of health. The nurse has also had time to follow up the known cases of tuberculosis. The town people have been eager to cooperate in this work and to appropriate money for its support. RICHARD M. SMITH.

BACTERIOLOGY AND PATHOLOGY

Newer Investigations on the Thymus Gland and Their Importance for Pediatrics

(*Heinrich Klose: Arch. f. Kinderh., 1911, lv, Nos. 1 and 2, p. 1*)

The article is divided into two parts: 1. A review of the literature and of our present knowledge on the subject of the thymus gland. 2. An account of the author's experiments on the subject of the function of the thymus.

1. The author reviews the literature and the two theories as to the cause of the symptoms associated with an enlarged thymus; i. e., (1) that such symptoms are due to a pressure of the thymus on the trachea; (2) that an enlarged thymus is merely one part of the general condition of lymphatism, with which is associated a weak heart, and that to the latter are due the symptoms of asphyxia and collapse.

2. Klose then reviews the reports of twenty-three patients operated on by different surgeons. Of these nineteen recovered entirely, three died, one was improved. He considers that operation is indicated whenever the diagnosis of an enlarged thymus with pressure symptoms can be made.

The symptoms of an enlarged thymus may be classified as follows:

Subjective: (a) Symptoms of tracheal obstruction. These may begin as a stridor in respiration and develop later into a condition marked by sudden attacks of asphyxia brought on by any shock, physical or mental. Any of these attacks may prove fatal; sometimes the child dies in the first attack; (b) difficulty in swallowing from pressure on the eosophagus; (c) symptoms of compression of the large vessels of the neck by the thymus.

Objective: On inspection there is a bulging in the jugular fossa on expiration. On percussion there is dulness in a triangular space, the base of which is the space between the sternoclavicular articulations, the apex at the second rib. The *x*-ray often decides the diagnosis, but a reliable picture is difficult to take in these children. The diagnosis must often be made in the absence of physical signs on symptoms of chronic tracheal obstruction with sudden attacks of asphyxia.

Treatment: Nonoperative measures are not recommended by Klose. Radiography he considers very dangerous, as its use may lead to a complete degeneration of the organ. Tracheotomy or intubation are not effective as the obstruction lies too deep.

Operations recommended are: 1. Intracapsular shelling out of the gland and ectopexy. This is done without removing any of the sternum; it is simple and is usually sufficient to cure the condition. If it is not sufficient, 2. Left sided enucleation or excision is recommended. 3. Finally, if necessary, thymectomy after removal of part of the manubrium sterni.

EXPERIMENTAL INVESTIGATIONS ON THE FUNCTION OF THE THYMUS

1. Review of other experiments.

Basch's experiments, principally directed toward the study of the relation between ossification and the thymus, the author reviews at length. Basch operated on twenty dogs, between 3 and 4 weeks old, removing the thymus as completely as possible. In thymectomized animals, as compared to normal control animals, he found, 1. The bones remained longer in the cartilaginous state and were more pliable. 2. A greater excretion of calcium from the kidneys. 3. A greater irritability of peripheral nerves. Convulsions were quite frequent in these dogs.

Klose criticises these experiments on the ground that the thymectomy should have been performed at the height of thymus development. This, in the dog, is at about the tenth to the twentieth day of life. After this time it undergoes rapid involution until the second and third month. A thymectomy performed during the stage of involution would give misleading results.

2. The Author's Experiments.

His own experiments were carried out on fifty-four animals. About the tenth day the thymus was removed as completely as possible. The symptoms appearing in the thymectomized animals he divided into stages as follows:

1. Latent period without symptoms lasting a variable time.

2. Stage of adiposity, lasting two to three months. The dogs increase in weight as rapidly as the normal animals, becoming very fat, though the fat is spongy and pasty. He compares the condition to that summed up by the term "exudative diathesis" in children. The appetite of the animals is enormous, and the tastes abnormal.

3. Cachexia thymopriva, lasting three to six months, sometimes as long as fourteen months. The dogs now lose in weight and become very weak, especially in regard to the bones. Spontaneous fractures are common. These dogs are completely idiotic and eat anything.

4. Coma thymicum. The animals finally become comatose and die.

The bone changes he describes in detail, showing, as he says, the characteristics of rachitis, osteomalacia and osteoporosis. In growing bones the changes are those of lessened growth, with abnormal softness and pliability, resembling rachitis; in adult bones the changes are those of an increased katabolism; that is, osteomalacia and osteoporosis. Cyst-formation is present in the spongy tissue of the bones. The epiphyseal cartilage is thickened. Microscopically, together with the osteoporosis, is seen an overgrowth of cartilaginous tissue and a lessening of calcium formation.

Chemically examined the bones are found to contain only 32 to 34 per cent. of calcium, while normal bones contain 65 per cent. The relation between the calcium carbonate and the calcium phosphate is the same in the thymectomized as in the normal animals.

The author then inquires into the relationship between the thymus gland and the development of bones. He proposes the theory that the bone changes after thymectomy are due to an "oxypathy" or intoxication with an acid, which he thinks is probably nucleinic acid. He concludes that the thymus is an organ which either hinders the formation of acid in the organism or neutralizes or masks a surplus of acid.

Neurologically, Klose found in the thymectomized animals a hyperirritability of the peripheral nerves. In those animals the injection of a large amount of calcium decreased this irritability. Intravenous injection of thymus extract caused in normal animals an increased irritability, soon returning to the normal. In thymectomized animals such an injection caused no increased excitability but an increase in all the pathologic symptoms. The brains of the experimental animals he found to be swollen and edematous. The spleen is the most important compensatory organ for the thymus: in the experimental animals it shows great richness in follicles and cell divisions. Dogs in whom the thymus is removed in its involution stages show only slight changes; if, however, the spleen is removed, the dog dies.

G. L. MEIGS.

METABOLISM AND NUTRITION

Influence of Sugar on the Intestinal Flora of Children

(*E. Hartje: Jahrb. f. Kinderh., xxiii, No. 5, p. 557*)

Sugar plays an important rôle in the formation of acids through bacterial activity, and therefore also in the change in reaction of the bowel contents, at least, in that part of the bowel in which the change from alkalinity to acidity takes place; therefore, it is well to know the amount of sugar in the bowel contents. Hartje examined the feces for sugar, the Haines test proving the most reliable, and found it present in the feces of all normal breast-fed children. Sugar was found present in most cases when the Trommer, Nylander and Ozason tests were used; therefore he concludes that sugar is always present in the feces of normal breast-fed children, although the amount may be small, in fact, at times only a trace. The large bowel always contained sugar, and the further from the cecum the contents were tested, the greater was the amount of sugar found. Sugar was never found in the feces of children fed on cows' milk unchanged, but when this was diluted, not less than 6 to 7 per cent. of sugar being added, sugar was always found in the feces, the amount depending on the quantity ingested. When milk-sugar was added, or malt-sugar in the form of malt extract (powdered), the reaction was far more apparent than when grape- or beet-sugar was added. It is assumed that the reason for this is that the milk-sugar and malt extract were excreted in larger quantities than the grape- and beet-sugar.

A quantitative examination was made in the case of two children, one aged 1 year and 3 months and the other 1 year and 5 months. The first child suffered from acquired chronic internal hydrocephalus and the second was severely rachitic. Neither child suffered from any notable digestive disturbances. Both children were fed with a cream, milk and water mixture, to which 7 per cent. of sugar was added. The composition of the mixture corresponded to that of mother's milk. One liter contained 200 gm. cream (with 15 per cent. fat), 100 gm. cows' milk, 700 gm. water and 56 gm. sugar. Beet-sugar, milk-sugar and malt-extract, in powdered form, were used. The observation extended over a period of six days. The feces of the last three days were collected, dried over the water bath, and the sugar-content estimated according to the method of Volhard-Pflüger. The first child ingested 1,200 gm. of the mixture daily; the second 1 liter. Sugar was never found present in the urine. The results of the examination of the analyses were as follows: when a 7 per cent. solution of sugar is given, sugar is found in the feces in sufficient amount to make a quantitative estimation. When like amounts of various kinds of sugars are given, it is found that the least sugar is excreted following the ingestion of beet-sugar, a larger amount when milk-sugar is given, and the greatest amount when malt-extract is given. In the case of each of these sugars, sugar is found in the feces in relative as well as absolute quantities, the least amount being found in the case of beet-sugar, a larger amount in the case of milk-sugar, and the largest quantity in the case of the malt-extract. Relatively, that is, in a definite amount of dried feces, there is ten times more sugar when malt-extract is given than when beet-sugar is given, and from five to seven times more when milk-sugar is given than when beet-sugar is given. The weight of the dried feces varies according to the kind of sugar administered. It is greatest when malt extract is given and lowest when milk-sugar is given. The author suggests that differences in resorption may account for these findings, or the action of the sugar on the intestinal mucosa may have something to do with it. The character of the stool varies with the kind of sugar given. Beet-sugar seems to cause a dry stool of alkaline reaction, whereas in the case of milk-sugar and malt-extract the stool is mushy and neutral or acid in reaction. The author concludes that in rickets the resorption of sugar is lowered considerably and that, therefore, it appears in greater amounts in the feces than under normal conditions. A microscopic examination of the feces in the case of these two children showed that Gram-positive bacteria were present in increased numbers and in the plate cultures the acidophil bacteria loomed up conspicuously. Sugar, then, apparently favors the growth of the acidophil organisms, provided that the sugar exceeds the albumin six to seven times. An increase in the albumin-content influences the intestinal flora to the extent of diminishing the number of acidophil organisms. The growth of these organisms is more especially favored when milk sugar or malt extract is administered. Beet-sugar and grape sugar apparently have a less favorable action on the growth of these organisms, although there is still an increase in their number. In the case of milk-sugar and malt extract, almost a pure culture of acidophil bacteria is obtained. When beet-sugar and grape-sugar are given the Gram-positive bacteria are present in greatest amount and bacteria other than the acidophils are found, so that the bacteriologic factor varies according to the kind of sugar given. The author does not confirm Sittler's findings in every particular. For instance, Sittler found that when he gave cane-sugar there was a rapid falling off in the number of *B. bifidus*, with a correspondingly rapid increase in the number of *B. birefringens*. The stool also became soapy and white in color. The author ascribes these occurrences, not to the kind of sugar given, but to the lessened amount of sugar to be found in the bowel. Bahrdt and Beifeld claim that milk-sugar influences the bifidus flora and that it is not only the absolute amount of sugar but the relative amount which is a determining factor, inasmuch as the casein is antagonistic. The author concludes that milk-sugar and malt-extract favor the growth of the acidophil organisms; they also soften the stool, make it more sour and lower the normal processes in the bowel to such an extent that little or no indican is found in the urine. In order to secure the characteristic bowel-content and the feces of the breast-milk-fed child, milk-sugar, and especially malt-extract, should be given.

ACUTE INFECTIOUS DISEASES

Meningitis in Infancy

(*John Lovett Morse: Boston Med. and Surg. Jour., 1911, clxiv, 701*)

When cerebrospinal meningitis is not epidemic at least 70 per cent. of the cases in infancy are tuberculous. A large majority of the others are meningococcal in origin. Meningitis due to other organisms is rare, and unless it develops during the course of some other disease, need not be considered in differential diagnosis. Meningitis secondary to otitis media almost never occurs in infancy. Symptoms of meningeal irritation are very common in the course of many diseases in infancy. If the fontanelle is open and not bulging the condition is almost surely not meningitis. If the fontanelle is closed a positive diagnosis can only be made by lumbar puncture. In general whenever there is any question as to the presence or absence of meningitis a lumbar puncture should be done. The symptomatology of meningitis in infancy is different from that in older children. The pulse and respiration are increased. Vomiting is common but is rarely explosive. Constipation is rare. Convulsions and manifestations of pain are unusual. Kernig's sign and knee-jerks are variable. Ankle-clonus, retraction and spasm of the abdominal muscles are usually absent. The diagnosis between tuberculous and cerebrospinal meningitis is very difficult. On the whole, the symptoms are more marked in the cerebrospinal than in the tuberculous form. It is the exception to find evidence of tuberculosis elsewhere in the body. A positive history of exposure to tuberculosis is of great value A leukocytosis is in favor of the cerebrospinal form but does not exclude the tuberculous. The tuberculin test, if positive, is strong evidence for tuberculous meningitis; a negative test is not conclusive. Lumbar puncture should be done in every case. In tuberculous meningitis the fluid runs out under increased pressure; is clear or slightly turbid; shows a fibrin clot on standing; contains more than twenty cells to the c.mm., mostly mononuclear; shows tubercle bacilli in about 90 per cent. of the cases. In cerebrospinal meningitis the fluid is under pressure; is turbid or purulent, shows a fibrin clot or deposit of pus on standing; contains many cells—mostly polynuclear; shows the diplococcus intracellularis. In acute poliomyelo-encephalitis the spinal fluid is like that in tuberculous meningitis but contains no bacilli. Tuberculous meningitis is very irregular in onset and early symptoms. In general the early symptoms are referable to the digestive tract. The course is usually short—averaging about two and one-half weeks, and progressively downward. Extreme meningeal symptoms are unusual. It is unfair to hold out the slightest hope of recovery. Treatment is symptomatic, with repeated lumbar puncture to relieve the cerebral pressure.

Cerebrospinal meningitis shows the same types as in adults. The most common sequel is hydrocephalus. Recovery is almost certain, unless the disease is of the malignant type, if the treatment is begun within the first two or three days. Flexner's serum should be injected directly into the spinal canal and in some cases into the ventricles. Serum should be given daily, in severe cases twice daily, until all the organisms have disappeared from the fluid, and longer if the fluid is markedly purulent. Elevation of temperature or rigidity of the neck alone are indications for continuance of the injections.

Pneumococcus meningitis is one of the manifestations of a general pneumococcus infection. The spinal fluid is turbid or purulent; contains an excess of polynuclear cells; shows the pneumococcus. The course is very short and almost always ends in death.

Influenza meningitis does not cause a leukocytosis of the blood. The spinal fluid is turbid or purulent; contains many polynuclear cells; shows many organisms. The course is short; prognosis almost invariably hopeless; treatment symptomatic. RICHARD M. SMITH.

TUBERCULOSIS AND SYPHILIS

The Beneficial Effect of Salvarsan in Syphilis of Childhood

(*Johann and Zoltan von Bokay and Ludwig Vormes: Wien. klin. Wchnschr., 1911, xxiv, No. 17, p. 583*)

Twenty-six patients with syphilis were treated with salvarsan. Thirteen of them were under 1 year, four between 1 and 2 years, one between 2 and 3, two between 4 and 5, two between 8 and 9 and four between 10 and 11 years of age. Only three of these children had acquired syphilis. Of the twenty-three children with hereditary syphilis, thirteen were under 1 year old; five under 2 months, four between 2 and 3 months and four over 3 months. All thirteen were well developed and well nourished, and all were breast-fed. The amount of salvarsan, given intramuscularly and subcutaneously, varied from 0.005 to 0.01 gm. for each kilogram of body weight. A second injection was given to ten children from 3 to 5 weeks after the first, whenever symptoms did not improve rapidly and the Wassermann reaction remained positive. All these patients have been watched from two to four months since being treated and results have been uniformly good. Yet these observers believe that a longer time must elapse before they can be sure of the lasting effect of salvarsan.

MAURICE OSTHEIMER.

GASTRO-INTESTINAL SYSTEM

Treatment of Intussusception in Children

(*W. E. Ladd: Boston Med. and Surg. Jour., 1911, clxiv, 712*)

The mortality of intussusception untreated is between 90 per cent. and 100 per cent.; treated with irrigation, inflation and enemata 70 per cent. to 80 per cent.; operated on 31 per cent. The prolonged use of irrigation or delay before operation is responsible in part for the high mortality with laparotomy. There is still some difference of opinion about the advisability of irrigation as a preliminary or aid to operation. It seems worth trying. It should be done with the patient anesthetized. In case there is any tumor felt after injection it is safer to operate at once. Rapidity in operation is important. The patient must be kept warm. A good-sized median incision is the best. Reduction is often difficult but should be done if possible as the mortality of resection is high. Feeding should be begun as soon as possible after the operation.

RICHARD M. SMITH.

Intussusception in Children

(*James Herbert Young: Boston Med. and Surg. Jour. 1911, clxiv, 710*)

Of all causes of intestinal obstruction at all ages intussusception comprises one-third, while in infants it comprises three-fourths. Invaginations are most common at the junction of the large and small intestine; they are usually single, but may be double or even triple. The frequency of this condition in infants is due probably to anatomic peculiarities—the long mesentery, the thin intestinal wall, the greater mobility of the cecum and ascending colon. At about the fourth month, the angle between the ileum and cecum which, until this time, is a right angle, changes so that the long axes of the two become more nearly parallel. With the anatomic changes there are certain disturbances of function, most important of which is exaggerated peristalsis. Vigorous stimulation of one part of the intestine produces an annular contraction. This contraction ring is drawn into the bowel above, and the progress of the intussusception is always at the expense of the outer portion. The contraction ring remains constantly at the head of the intussusceptum. The only exception to this rule is in the ileocecal variety in which the growth of the invagination is at the expense of the inner coil of intestine. The important symptoms are pain, vomiting, bloody stools and palpable tumor (in 80 per cent. of cases). Acute diarrheas with bloody stool must be excluded. The treatment should be immediate laparotomy.

RICHARD M. SMITH.

Chronic Intestinal Indigestion

(*J. P. Crozer Griffith: Arch. Pediat., xxviii, 324*)

Griffith emphasizes that medical treatment of chronic intestinal indigestion in early life is largely of secondary importance. The overcoming of the constipation, which is such a common symptom, is important. In addition to the hygienic measures, either small daily doses of a saline laxative or of cascara, phenolphthalein or similar drug, may be required. In other cases a small amount of sulphate of magnesia or syrup of rhubarb may be added to the tonic medicines administered. In bad cases the nightly injection of olive oil or cotton-seed oil may be of service. Very often the diet may be selected to overcome the constipation, bearing in mind, however, that many of the laxative foods are more or less irritating to the bowels. As a rule, enemata are not efficient, as they operate only on the rectum. A drug is required which affects the whole of the intestinal tract. When there is much secretion of mucus from the bowel, saline douching is sometimes of service, but this practice should not be continuous, as it sometimes maintains the symptoms which it is intended to cure. The administration of a good malt extract appears to aid the digestion of starch. One should be selected known to contain a large percentage of diastase, as there is a great difference among them in this respect. In general, as far as other medicinal treatment goes, Griffith has had the best results with the combination of an alkali with a bitter tonic. For this purpose, bicarbonate of soda may be given with tincture of nux vomica, compound tincture of gentian, and an aromatic water, administered ten to twenty minutes before meals. Cod-liver oil, although theoretically an excellent remedy to improve the general health, is often contraindicated, expecially early in the disease, on account of its tendency to increase indigestion in many cases. The remark applies to the use of iron given for the anemia, since until convalescence is established, this may increase the digestive trouble and the constipation. The importance of resistance in the treatment is emphasized. Griffith says that unless this is maintained, and especially unless the dietetic treatment is rigorously followed for months, an improvement which has seemed very decided, and even a cure which has seemed complete, will inevitably be followed by relapse. F. C. Z.

BLOOD AND CIRCULATORY SYSTEM

Blood-Pressure in Acute Nephritis of Children

(*Lennox Gordon: Arch. Pediat., xxviii, 343*)

According to Gordon, the blood-pressure in children suffering from acute nephritis is raised, and this rise of pressure may be very great. In three of seven acute cases, the hypertension was very marked. This fact is of diagnostic value, as in no other disease of childhood is there to be found the same high range of blood-pressure. Those patients who had the highest pressure were those in whom only a slight trace of edema was noticeable, and also it is of interest to note that in these same patients the quantity of blood in the urine was very great, the urine, indeed, looking like pure blood; the explanation of the large quantity of blood in the urine being, probably, that a rupture of the renal capillaries had occurred consequent on the greatly increased blood-pressure. Gordon emphasizes the fact that in children it is only by means of the sphygmomanometer that changes in the blood-pressure can be ascertained with any degree of certainty. F. C. Z.

NERVOUS SYSTEM

Migraine in Children Due to Disturbances of the Function of the Thyroid Gland

(*Leopold Levi and H. de Rothschild: Rev. d'Hyg. et de méd. inf., 1911, x, 2, p. 113*)

Leopold Levi and H. de Rothschild again discuss the disturbances of thyroid secretion as a cause of migraine. They believe that in adults 75 per cent. of all cases of migraine are due to thyroid instability, while in children all cases are due to this cause. Ten cases in children between 9 and 15 years are reported. Under thyroid treatment these cases have either been cured, when treatment has continued a long enough time, or have been relieved while under treatment and had a return of symptoms when the treatment was omitted. Although in these cases there were seven boys and three girls they think that in children the two sexes are equally affected. In more than half the cases the condition was hereditary. The powdered gland was given in doses of 5 milligrams, 25 milligrams and 10 centigrams, usually once or twice a day. Relief of symptoms with a small dose may be followed by a return of symptoms when the dose is increased. In certain cases some symptoms were wholly or partially relieved, while others were uninfluenced by treatment. The intense, paroxysmal headache with vomiting was at times transformed into a simple headache. Urticaria, eczema and psoriasis, associated with migraine, were cured. Cases which showed evidences of both hyper- and hyposecretion were equally benefited. For permanent cure treatment must extend over a long period of time, even up to two years. J. Herbert Young.

CORRESPONDENCE

IMPORTANT CORRECTION IN DR. WALTER BREM'S PAPER ON INFLUENZAL MENINGITIS IN JUNE, 1911, ISSUE

To the Editor: In the AMERICAN JOURNAL OF DISEASES OF CHILDREN, June, 1911, I published, with Zeiler, a report of two cases of influenzal meningitis. We stated that Wollstein in her paper on the same subject (*Am. Jour. Dis. Children*, January, 1911) had failed to include one of her own cases in her summary of the literature. Dr. Wollstein in a recent conversation with me pointed out that she had included the case under the names of Agar and Avery, who had previously made a report of it, as she stated elsewhere in her paper.

I regret very much that the oversight on my part occurred, and shall be obliged if you will publish this correction.

WALTER BREM, M.D.,
Colon Hospital, Cristobal, Canal Zone.

American Journal of Diseases of Children

Vol. 2 AUGUST, 1911 No. 2

THE OCCURRENCE OF INFANTILE PARALYSIS IN THE UNITED STATES AND CANADA IN 1910 *

ROBERT W. LOVETT, M.D.
BOSTON

The great prevalence of infantile paralysis in the United States in 1910 and its rapid increase in the last two or three years in this country, are matters which demand our serious consideration, and in the following paper will be presented the data obtainable on the subject, preceded by a brief résumé of the history of the disease in this country insofar as it bears on the present situation.

That infantile paralysis is not a new disease is a matter of common information, and it is of interest to note that the first probable allusion to it to be found in literature occurs in the book of Samuel, fourth chapter and fourth verse. It is as follows:

> "And Jonathan, Saul's son, had a son that was lame in his feet. He was five years old when the tidings came of Saul and Jonathan out of Jezreel, and his nurse took him up and it came to pass as she made haste to flee that he fell and became lame. And his name was Mephibosheth."

This short clinical history, although suggestive, is hardly convincing, but it is quite as likely to have been a case of infantile paralysis as are some of the cases reported as such in the year 1910.

The disease is first recorded as occurring in America in epidemic form in 1841 by Colmer,[1] as follows:

> "While on a visit to this parish, West Feliciana, Louisiana, in the fall of 1841, my attention was called to a child, 1 year old, slowly recovering from a hemiplegia. The parents, who were people of intelligence and unquestioned veracity, stated that either eight or ten cases of either hemiplegia or paraplegia had occurred during the preceding three or four months within a few miles of their home. Some of these recovered completely, others were improving. The little sufferers were all under 2 years of age and the cause seemed to be the same in all, viz., teething."

The account of this epidemic has, however, been questioned on the ground that it was only hearsay evidence and not substantiated, and the first authentic description of an epidemic of thirteen cases is credited to Bergenholz, a Swede, in 1881.

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*Presented by invitation before the American Pediatric Society, Lake Mohonk, N. Y., June 1, 1911.

[1] Am. Jour. Med. Sc., 1845, v, 248.

That infantile paralysis has existed in the United States for an indefinite time is perfectly familiar to us from the fact that we all know of adults affected whose history would reach back fifty years.

In 1875, Sinkler[2] reported that in the preceding four years he had seen eighty-six cases at the Infirmary for Nervous Diseases in Philadelphia.

The best evidence that I can find of the existence of infantile paralysis in our midst in any considerable degree for the last twenty-five years is derived from a study of the records of two hospitals, one in Boston and one in New York, which also contribute the best evidence that I have seen of the sudden increase of the disease in our midst in the last few years. The first named of these hospitals draws from a large area and the clientele of both in the last twenty-five years has been more or less constant.

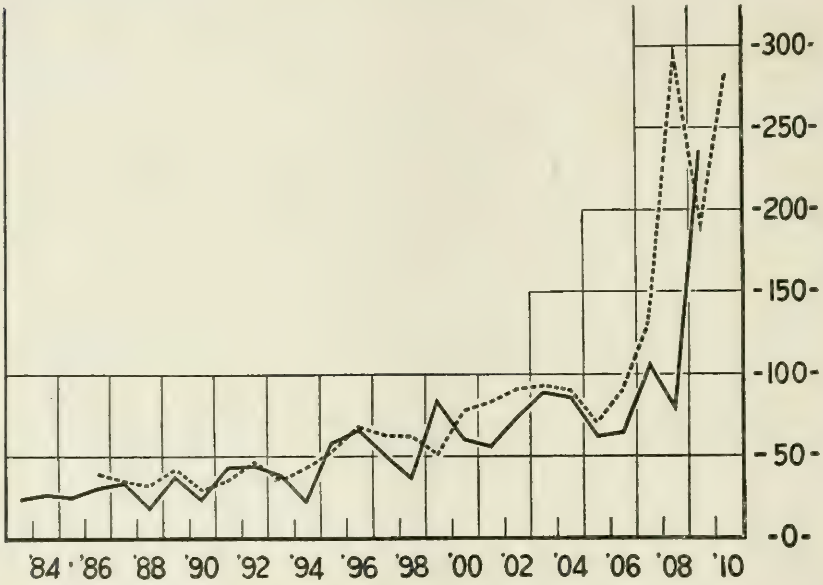

Chart 1.—Number of new patients with infantile paralysis treated at Children's Hospital, Boston, indicated by the solid black line; those treated at the New York Orthopedic Dispensary and Hospital by the dotted line; both by years.

The accompanying chart (Chart 1) is constructed in part from the records of the orthopedic out-patient department of the Children's Hospital, Boston, and shows the number of new patients with infantile paralysis applying for treatment since 1883 in that department. The figures show that in 1883 we treated twenty-two patients, and that the number of cases with unimportant fluctuations rose steadily for twenty-five years, until 1909, when Boston was an epidemic center, when it rose suddenly to 235 cases.

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[2] Sinkler: Boston Med. and Surg. Jour., Nov. 23, 1893.

The second institution analyzed on the chart is the New York Orthopedic Hospital and Dispensary, the figures of which were kindly furnished to me by Dr. Russell A. Hibbs, and which show in general the same facts. There were thirty-nine new cases in 1886, rising gradually to 1907, when a marked increase occurred. It will be noted that the New York increase began two years before that in Boston.

The first outbreak in the United States of the disease in any considerable degree was in 1894, when Caverly[3] of Rutland described an epidemic of 132 cases in the Otto Creek Valley, Vermont. In this epidemic Caverly attended to abortive cases, not under that name but as cases presenting the clinical symptoms without the paralysis.

In the same year was reported by Brackett[4] a group of ten cases in North Adams, Massachusetts. Both Rutland and North Adams are in railroad communication with Boston, and it is interesting to note that Putnam[5] in November of the previous year, 1893, had called attention to the increased prevalence of the disease in Boston in the preceding summer, the patients coming from different parts of the suburbs of Boston.

In the following eleven years, that is, from 1894 up to 1904, there were reported in the United States nine small epidemics (Chart 2), the second largest again in Massachusetts, consisting of thirty-eight cases,[6] and the largest, fifty-five cases,[7] in California, about San Francisco. The total epidemic cases reported in these eleven years, i. e., from 1894 to 1904, inclusive, in the United States were 157, or an average of about fifteen a year.

In 1905-6 no epidemics were reported.

In 1907 the most extensive epidemic ever known visited New York City and its surroundings and was estimated at 2,500 cases. In the same year were reported epidemics in Virginia (26 cases), Pennsylvania (100 cases), Massachusetts (234 cases), Michigan (20 cases), and Northern New York (29 cases); a total of about 2,900 cases.

In the year 1908 the disease was apparently quiescent, groups of cases being reported from Massachusetts (136), Michigan (30), Florida (16), Minnesota (60) and Wisconsin (60); a total of 302 cases.

In the year 1909 large epidemics occurred in Massachusetts, Minnesota, Kansas, Nebraska and Cuba, the total number of cases being 2,343.

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[3] Jour. Am. Med. Assn., 1896, xxvi, 1.

[4] Brackett: Tr. Am. Orthop. Assn., xi, 132.

[5] Putnam: Boston Med. and Surg. Jour., Nov. 23, 1893.

[6] Painter: Boston Med. and Surg. Jour., cxlvii, 633.

[7] Wood's Occidental Med. Jour., xvii, 77.

When we come to the analysis of the figures for 1910 we must remember that they were brought out by a systematic and extended inquiry undertaken by the Massachusetts State Board of Health, and probably had such an inquiry been possible in one of the earlier years a larger number of cases would have been discovered than now stand as reported in those years. Still, one cannot conceal the fact that in 1910 there apparently occurred a very much larger number of cases than before all over the United States, and that the extent and distribution of the disease in this country in 1910 was of a different character from that of any previous year.

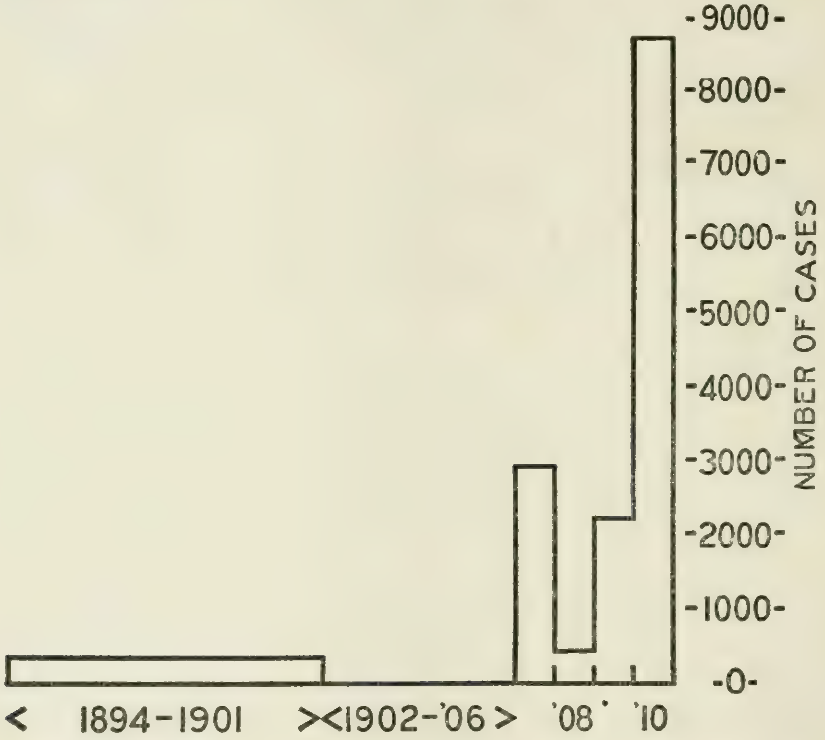

Chart 2.—Prevalence of infantile paralysis in the United States, 1894 to 1910.

There were about 8,700 cases reported in the United States in 1910, and if we contrast that figure with the years prior to 1904 when the average yearly number was fifteen cases per year we may appreciate what an enormous increase has occurred.

To summarize for a moment our facts so far collected: The disease has unquestionably existed in this country for many years. In 1893 the first reported tendency to increase is said to have showed itself in Boston, followed by the Vermont epidemic in 1894, and in the next eleven years by other small epidemics in various parts of the country.

Then came a period of quiescence followed by a violent outbreak in New York in 1907, since which, on the whole the extension of the disease has been rapid and in all directions. We are evidently now facing conditions favorable to the spread of the disease which did not exist in former years, and conditions which do not exist in Europe now, and it is for the purpose of bringing out this very point that I have thus dwelt on the earlier history of the disease in this country.

In Europe, although there has been an undoubted tendency of the disease to spread since 1905, when the great Scandinavian epidemic occurred, five-sevenths of 8,000 cases reported from all over the world for the five years ending in 1909 occurred in this country. The relative prevalence of the disease on the two continents is shown in the chart (Chart 3) and needs no comment. The disease is a reportable one in Sweden, Norway, Germany and Austria, so that in these countries, in any event, epidemics are not likely to fail to be reported.

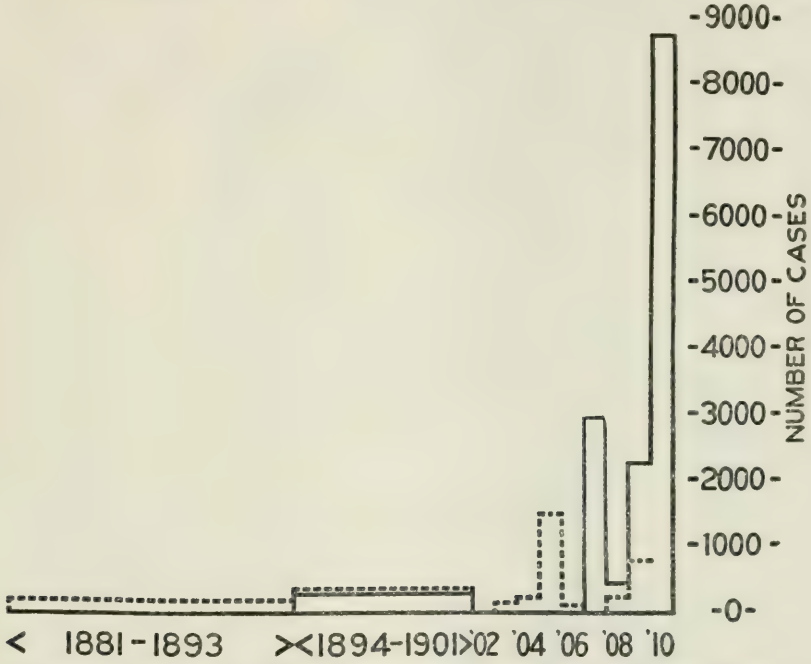

Chart 3.—Relative prevalence of infantile paralysis in the United States and Europe and Australia; the solid black line refers to the United States; the dotted line to the following countries: Italy, Sweden, Norway, Germany, Austria, France, England and Australia.

The data with regard to the disease in the United States in 1910 were collected as follows: Dr. M. W. Richardson, the secretary of the Massachusetts State Board of Health, sent out several hundred letters of inquiry to state boards of health, to officers of state medical societies

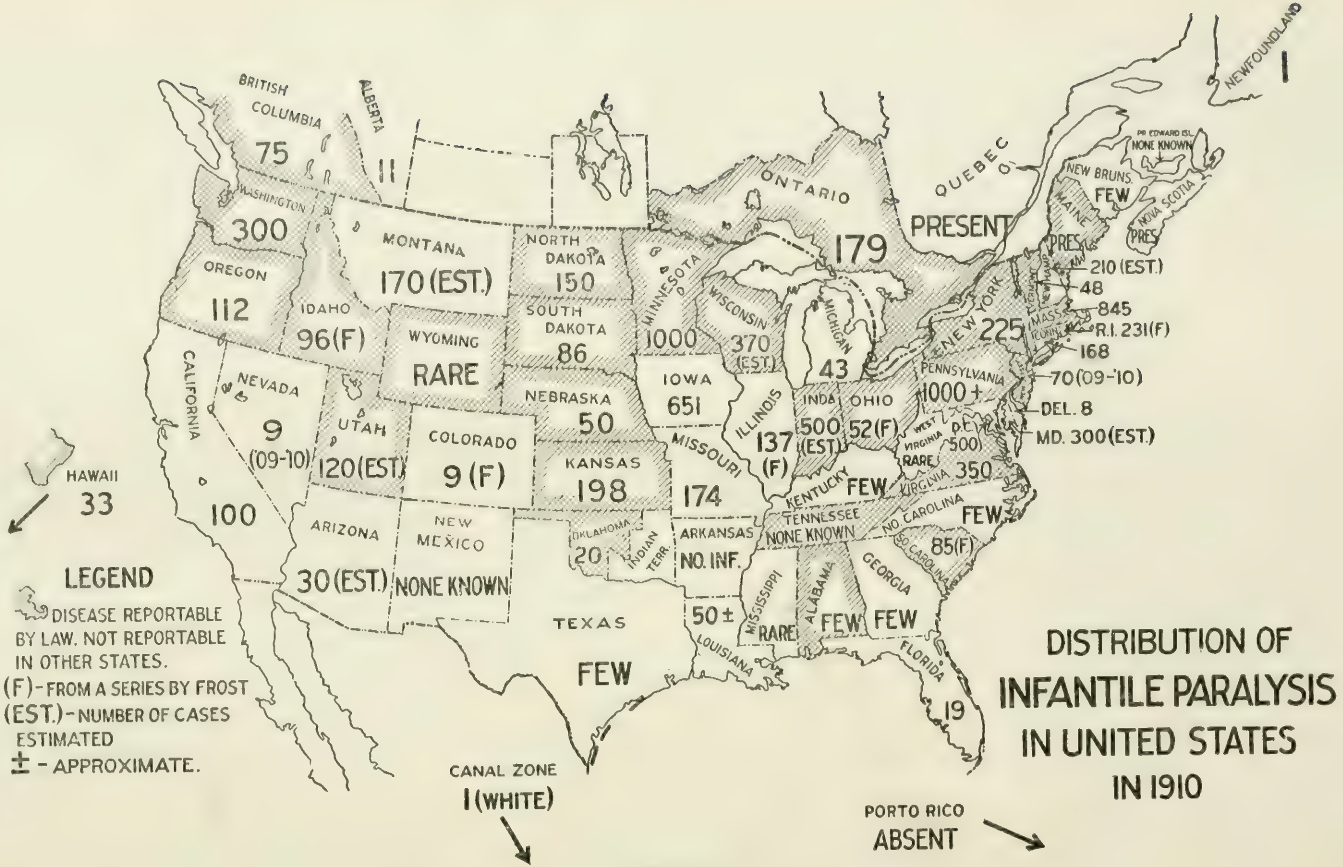
DISTRIBUTION OF
INFANTILE PARALYSIS
IN UNITED STATES
IN 1910
LEGEND
DISEASE REPORTABLE BY LAW. NOT REPORTABLE IN OTHER STATES.
(F)-FROM A SERIES BY FROST
(EST.)-NUMBER OF CASES ESTIMATED
± - APPROXIMATE.
HAWAII
33
BRITISH COLUMBIA
75
ALBERTA
11
WASHINGTON
300
OREGON
112
CALIFORNIA
100
IDAHO
96(F)
NEVADA
9
(09-10)
MONTANA
170(EST.)
WYOMING
RARE
UTAH
120(EST.)
ARIZONA
30(EST.)
COLORADO
9 (F)
NEW MEXICO
NONE KNOWN
NORTH DAKOTA
150
SOUTH DAKOTA
86
NEBRASKA
50
KANSAS
198
OKLAHOMA
20
INDIAN TERR.
TEXAS
FEW
MINNESOTA
1000
IOWA
651
MISSOURI
174
ARKANSAS
NO. INF.
50 ±
LOUISIANA
WISCONSIN
370
(EST.)
ILLINOIS
137
(F)
MICHIGAN
43
INDA
500
(EST.)
OHIO
52(F)
KENTUCKY
FEW
TENNESSEE
NONE KNOWN
MISSISSIPPI
RARE
ALABAMA
FEW
GEORGIA
FEW
FLORIDA
19
ONTARIO
179
QUEBEC
PRESENT
NEWFOUNDLAND
1
PR. EDWARD ISL.
NONE KNOWN
NEW BRUNS.
FEW
NOVA SCOTIA
PRES.
MAINE
PRES.
VERMONT
NEW HAMP.
MASS.
CONN.
210 (EST.)
48
845
R.I. 231(F)
168
70(09-'10)
DEL. 8
MD. 300(EST.)
NEW YORK
225
PENNSYLVANIA
1000 +
WEST VIRGINIA
RARE
D.C.
500
VIRGINIA
350
NO. CAROLINA
FEW
SO. CAROLINA
85(F)
CANAL ZONE
1 (WHITE)
PORTO RICO
ABSENT

Chart 4

and to prominent physicians in various parts of this country, its dependencies, and Canada. From their replies to those letters the data given in Table 1 have been compiled. In a few instances the figures have been taken from the Marine Hospital Service tables prepared by Frost, and such are marked (F). In certain instances where no reliable number of cases or no number at all was given in a state, and the number of deaths from infantile paralysis during 1910 was given, the number of deaths has been multiplied by ten, a conservative mortality per cent., and the number of probable cases thus estimated. In such cases the figures have been followed by the abbreviation (Est.).

TABLE 1.—DISTRIBUTION OF INFANTILE PARALYSIS IN THE UNITED STATES, 1910

Alabama*	Few	North Carolina	Few
Arizona	30 Est.	North Dakota*	150
Arkansas	No information	Ohio*	52 F.
California	100	Oklahoma*	20
Colorado	9 F.	Oregon*	112
Connecicut	168	Pennsylvania*	1000+
Delaware	8	South Carolina*	85 F.
District of Columbia	500	Rhode Island	231 F
Florida	19	South Dakota*	86
Georgia	Few	Tennessee*	None known
Idaho*	96 F.	Texas	Few
Illinois	137 F.	Utah*	120 Est.
Indiana*	500 Est.	Vermont*	48
Iowa	651	Virginia*	350
Kansas*	198	Washington*	300
Kentucky	Few	West Virginia	Rare
Louisiana	50 Approx.	Wisconsin*	370 Est.
Maine*	Present	Wyoming*	Rare
Maryland	300 Est.		
Massachusetts*	845	Hawaii*	33
Michigan	43	Porto Rico	Absent
Minnesota*	1000	Alberta	11
Mississippi	Rare	Canal Zone	1 White
Missouri	174	Philippines	None
Montana	170 Est	Newfoundland	1
Nebraska*	50	Nova Scotia	Present
Nevada	9 (1909-10)	Ontario*	179
New Hampshire	210 Est.	Prince Edward Islands	None known
New Jersey*	70 (1909-10)	Quebec	Present
New Mexico	None known	British Columbia*	75
New York*	225	New Brunswick	Few

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*Disease reportable by law. (In states not starred disease is not reportable by law.)

Est.—No of cases estimated.

F.—From series by Frost.

Approx.—Approximate.

Mortality per cents. have not been allowed any importance in this tabulation, as they are only of value or significance in instances in which an epidemic has been carefully enough studied to bring out the total number of cases occurring. For example, one state in which the disease is not reportable, reports thirty-five cases and thirty deaths, which probably does not mean that the mortality was enormously high in that state, but that the deaths were reported and the non-fatal cases were not.

Although somewhat lower than the figures in foreign countries, there is reason to believe that the Massachusetts figures of 8 per cent. are approximately correct for that state at least, although the mortality per cent. in the District of Columbia in 1910 was only about 3 per cent.[8]

The map of the United States (Chart 4), on which has been marked the number of cases in each state for 1910, shows a total of about 8,700 cases, not counting Canada or such dependencies as Hawaii, and making no account of states reporting "a few," etc. In practically all cases not otherwise designated, the number of cases given is the number officially given out. Various terms have been used in the cases of states from which exact information was not obtainable, the term being chosen according to the information which was sent in.

The disease is now reportable by law in twenty-three states, which are shown shaded on the map, and various other states have the matter under consideration or may have legislated very recently.

A study of this map shows in the first place a wide-spread and general distribution of the disease with, in general, a focal occurrence and radiation from these foci. There is in general a scarcity of cases in the southeastern section of the country. In the New England states there occurred a group of cases, the largest number being in Massachusetts and Rhode Island. It is probable that the large number credited to Massachusetts is in a measure due to the careful investigation of the disease carried on there now for four years, as a result of which the medical profession is on the alert to report cases, so that the apparent prevalence there is probably exaggerated in comparison with other states.

An epidemic focus of considerable size existed in Pennsylvania, Maryland, North Carolina and Virginia, the latter state being the southern limit of any considerable extension in the East.

In the Middle West there was a large epidemic focus in Minnesota, Wisconsin and Iowa, some 2,000 cases being reported from these states, and in a circle around these three seriously infected states there existed in neighboring states from fifty to 200 cases per state, with over 500 cases in Indiana. An area of comparative immunity from north to south covered the Rocky Mountain region, but on the Pacific Coast there existed in Washington an epidemic center of 300 cases, with extension south to California and general involvement of the Southwestern states.

In Canada the disease appeared most extensively in the Province of Ontario, with 179 cases, with seventy-five in British Columbia and eleven in Alberta. New Brunswick reported a few cases, but no deaths, and there were cases in Quebec and Nova Scotia, with one in Newfoundland, but Prince Edward Island reported the disease as unknown there in 1910.

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[8] Washington Med. Ann., May., 1911.

The disease is reportable by law in Ontario and British Columbia and not in the other provinces.

As to our Southern dependencies, there were no cases in Porto Rico or the Philippines; one in a white laborer in the Canal Zone, and an epidemic of thirty-three cases in Hawaii.

It is disquieting to note that in April of this year (1911) an epidemic of twenty or more cases occurred in Louisiana,[9] which was so threatening that the governor was appealed to for aid in suppressing the epidemic. In Massachusetts in the four years during which the disease has been under observation it has occurred earlier each year, reaching its height in September in 1907, August and September in 1908, in August in 1909 and in July in 1910. It will be of importance to note whether this is a mere coincidence or whether the disease is really tending to occur earlier as it spreads.

Such are the data that it has been possible to bring to light, but it is of course evident that the number of cases thus officially reported is a poor criterion by which to judge the total number that have occurred. In half of the states the disease is not reportable and it is naturally impossible to obtain any reliable information from these, and where it is reportable many cases are either unrecognized or unreported when recognized. The disease is so dreaded by the public that there will be a tendency to the suppression of information, especially in summer resorts.

In view of these facts, it may seem to this society worth while to take action to urge again on all state boards of health the importance of placing this disease on the list of those reportable by law. Several states in which the disease is not now reportable have the matter under consideration and the situation is too serious not to warrant every effort to place the disease where it may be studied and watched.

Several state boards have set on foot investigations as to the prevalence and distribution of the disease and have formulated blanks for distribution. But desirable as this is, we need more than this. The important questions that we want to have answered, the facts that will help us in finding out more about the disease, are not to be settled by the routine investigation of epidemics.

These are to be found in literature by the dozen, and anyone familiar with the subject can tell you in advance just what such an investigation will show. The disease will be found in scattered foci, with cases radiating from these foci. It will reach its height in the late summer; it will follow the lines of travel; it will affect mostly children in the first dentition; the mortality rate will be from 3 to 15 per cent. In October the epidemic will begin to die out. Data of this class exist in abundance and are useful only in giving us the distribution of the disease in a given locality.

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[9] New Orleans Times Democrat, April 27, 1911.

What we do need is a careful house-to-house study, made, if possible, during the epidemic by competent medical men on salary, giving their whole time to the work. These men should examine most carefully the premises, the neighborhood, and every detail of the patient's life, environment and habits, his points of contact with other cases, with sick animals, the history of wounds and insect bites, his food, antecedent illnesses, etc.

The solution of the mystery of this disease may come from the laboratory or from the field work, or from both, but field work to be of any use must be intensive. The collection of routine data will not settle the question of etiology.

Such a plan as this means financial support, and in Massachusetts we have found the legislature ready to give us such support, and not only the legislature, but the public, a voluntary subscription of $5,000 from private sources having been placed at the disposal of an expert for the study of animal diseases akin to infantile paralysis. In addition to this the Massachusetts legislature of this year has appropriated $10,000 for the use of the State Board of Health in the coming year in the study of the disease. These facts show how a community feels where the disease has prevailed extensively.

Finally, it would be of value if some bureau or central committee for the interchange of information could be established with regard to the disease in America and the provinces. Such data as are presented above are only secured now by the expenditure of much effort and a considerable amount of work and money. If the disease is to increase in the near future at the same rate as in the last two years in America, it is important for the medical profession to have at its disposal every facility for obtaining information and every opportunity for study of the disease that is possible. On the one side we run the risk of alarming the community by the publication of such facts as these, but on the other hand, if we neglect to look at the situation as its exists, we run the risk of being charged later with having underestimated the seriousness of the present situation.

234 Marlboro Street.

THE CEREBRAL FORMS OF POLIOMYELITIS *

HENRY KOPLIK, M.D.
NEW YORK

During the first epidemic of poliomyelitis and in the recurrent outbreaks in New York and vicinity there have occurred here and there a number of cases which have been of great interest because of their close simulation of certain cerebral conditions which I shall mention later. I refer to those cases of poliomyelitis which belong more particularly to the cerebral group of this affection. Polioencephalitis or encephalitis, as it is called, was first brought into closer relationship with poliomyelitis by Medin. In the large Swedish epidemic of 1905 there were many of these cases, and Medin in his early writings insisted on the general identity of this set of cases with poliomyelitis as it was then known. His assumptions were at first disputed by men of no less genius than Henoch, who thought that Medin in describing the cerebral forms of poliomyelitis as identical with the spinal forms in etiology and pathology had rather committed an error of clinical observation and mistaken his cases for something of another character. How certain and true the original observations of Medin have been time has shown, and Harbitz and Scheele have proven beyond question that the infectious agent producing epidemic poliomyelitis may extend to any part of the cerebrospinal system, and may affect both the gray and white matter of the brain and cord. Moreover, there is in all cases of poliomyelitis a real meningitis; that is, the processes of infection expend themselves on the membranes of the brain and cord. There is an inflammation and infiltration of these structures, and from the vessels of the pia the toxic or infectious agent enters the tissues of the brain and cord, there effecting changes of greater or lesser severity. Thus the consequent symptoms will differ in sets of cases according to the localization of the inflammatory processes at play.

The cases to which I especially desire to call attention are those in which the structures of the brain, medulla and pons are affected, leaving the cord for the most part unaffected permanently. These cases have been previously described by various writers as encephalitis or polioencephalitis superior or inferior of Wernicke or of poliomyeloencephalitis of Strümpel. We may group all these descriptive clinical pictures under the entity of polioencephalitis. This would also include the pontine forms of encephalitis of Oppenheim. The general picture

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*Read before the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

of polioencephalitis is cerebral, the symptoms are cerebral symptoms with, in certain cases, added palsies. Thus if the nuclei of the oculomotor nerves are affected we have with the cerebral symptoms an ophthalmoplegia of greater or lesser extent, identical with that which Wernicke describes as polioencephalitis superior. If the nuclei of the facial nerves are affected and the gray matter in the floor of the fourth ventricle, the cerebral symptoms are supplemented by facial palsies, and thus there is produced the picture described by Wernicke as polioencephalitis inferior. If the process extend still further down it may involve the nuclear masses of the hypoglossus and more vital nuclei, and then symptoms of paralysis identical with acute bulbar paralysis are produced. Certain it is that the forms of polioencephalitis will merge into one another. Thus, cases occur in which there are isolated palsies, such as those of the muscles, of one or other of the eyes; and then cases occur in which eye and facial nuclei (muscles) are involved, and others in which all these are affected and bulbar symptoms occur. The last group rather number the fatal cases, though I have seen a number of bulbar cases in which recovery occurred.

The cases which are limited in their extent of involvement of the ocular and facial nuclei, and which are accompanied by cerebral symptoms, are those which to me have been of greatest interest, because in such cases of polioencephalitis I have had the greatest difficulty, in the face of the cerebral symptoms, accompanied, as they were after a while, with nuclear palsies, to differentiate them from forms of meningitis either of the acute suppurative (meningococcic) variety, or the tuberculous forms of the disease. In fact, in some cases the clinical similarity of forms of polioencephalitis with forms of meningitis is so close that it is only by careful observation that we can differentiate the two, and then only with a possibility of some doubt. In order to facilitate clinical study of polioencephalitis it will be best to first draft in outline the general history of these cases.

A child in previously good health, without any marked prodromal symptoms, develops fever which may be quite high or may be moderate in degree. There may be complaint of some headache, there may be vomiting. Such a child will continue for twenty-four hours to be up and about, and after the initial period it is noted that the fever continues as does also the headache, and after a time the patient is too sick to be about, complains of a tired feeling and goes to bed. It is then noted that the sopor deepens, and then the temperature may subside to the normal or continue a little above the normal. In some cases from this time on the history is that the patient is at times delirious, irrational, complains of headache, and resents being disturbed. There is extreme hyperesthesia. Some patients complain of pain in the nape of the neck; there is marked rigidity with the Kernig sign in the lower extremities, and signs of a mild hydrocephalus (Macewen). Such patients may have a maudlin delirium, lie crouched in bed and refuse to take food. Close examination may discover isolated ocular palsy in some cases, and this is the only objective palsy present. In other cases with palsy of some of the ocular muscles there is slight facial palsy of one or the other side, and in still other cases these palsies may be combined with a very mild weakness of one or the other upper extremity. After a week or two, the patient gradually becomes more rational, the sensorium is brighter and he begins to recognize objects and talk rationally. If during the illness the patient is caused to stand, there is noticed a very marked ataxia and vertigo, with Romberg's symptom. As convalescence is established, the ataxia is the last symptom to improve. The hydrocephalus may persist, the compromised mental capacities may not return to the absolute normal as soon as one would expect. The temperature has during the illness, directly following the period of invasion, been normal, or, in exceptional cases, there may have been a rise of 2 or 3 degrees, with a fall to the normal daily for a week or more. As the patients convalesce they are able to sit up, this not having been hitherto possible. Speech is more distinct, due to the recession of the ataxia.

This is a sketch of the common picture. When recovery is established there may remain a strabismus, or a very mild form of ataxia in the gait, an uncertainty as it were. In one or two of my cases I have seen optic neuritis, such as choked disk, in the course of the disease, and this also may retrograde, the eyesight being entirely restored. In other cases, the eyesight which has failed during the illness may progress to absolute blindness, and this in turn may slightly improve, as in one of my cases, so that after a lapse of months the eyesight may have improved from absolute blindness to the ability to distinguish gross, large objects. In another group I have seen a complete unilateral ophthalmoplegia with dilatation of the pupil of the affected eye.

I have related enough of the symptomatology of this form of encephalitis or polioencephalitis to show how close the similarity to a cerebrospinal meningitis may be, the sudden onset, the high fever, the rigidity of the neck, the headache, the Kernig, all run close to the symptom-complex of a meningitis, and yet close study will show some differences. There is in polioencephalitis a short preliminary period in which the patient, having had a high fever, continues to be about. There is also an increasing sopor which extends over days; this is quite unlike the onset of a cerebrospinal meningitis. In these two points we can sometimes differentiate between the two diseases. Here, however, the dissimilarity ceases. In a recent outbreak of polioencephalitis in Staten

Island these two points stood out quite sharply on the clinical canvas, namely, the period of a day or so of high fever in which the patients did not quite take to bed, and then the period of fever and increasing sopor with the addition of all the symptoms of true meningitis.

Another set of cases of polioencephalitis are still more perplexing, inasmuch as they closely simulate another type of meningitis, the tuberculous form. A patient having been in previous good health will develop fever with some vomiting; the fever may be low, 102 or 103 F., or high, 104 to 105 F. The fever continues for a day or more and then sopor sets in, the temperature drops to the normal, the patient becomes completely unconscious. With this unconsciousness there is marked hydrocephalus, facial palsy, ocular palsy, such as strabismus, with loss of reflex at the knee, no Kernig, and a Babinski reflex. There may be a *tâche cérébrale.* After five or seven days of illness, the picture is the exact counterpart of a tuberculous case. The patient lies absolutely flaccid; there may be but very mild rigidity of the neck, there is Cheyne-Stokes respiration, and absence of reaction to mechanical stimuli in the presence of a normal or slightly raised temperature. After a few days the patient may succumb, but in many cases may come out of the coma and regain consciousness and power in the extremities. Such cases I have seen.

In another form the patient may have had a very short period of fever, which may have come on suddenly. Then after a few days the temperature falls to the normal, but the patient is noted to be stupid, and to act as if in a trance; there is mild hydrocephalus, but the sopor is the principal symptom. A bright child is noticed to act stupidly; begs to be left alone. There is hyperesthesia. All of these are present in face of a normal temperature. Gradually the patient after two or three weeks becomes brighter, takes an interest in surroundings, and the ataxia, which in some cases amounts to absolute inability to walk, in others to staggering gait with vertigo, gradually improves. The similarity of these cases to tuberculous meningitis is exceedingly close. There is one very salient point of difference. In cases of polioencephalitis the onset is sudden. It is especially noticeable that the children have previously been in excellent health, when they are attacked by the disease within twenty-four or forty-eight hours at the most. In this respect the two maladies are far apart. In tuberculous meningitis the onset is gradual, and cases of sudden onset are extremely rare; in fact, I have not seen an authentic case in several hundreds of cases. In tuberculous meningitis there is a state of sopor in which some preservation of intelligence and of the surroundings exists, which does not last long, but will deepen into coma; whereas in polioencephalitis there is a diminution of the sopor, and finally after a week or two the patient is observed to be brighter.

CASE REPORTS

CASE 1.—L. D., male, aged 5 years, has had rachitis. Three years ago he had scarlet fever and diphtheria. The tonsils had been removed.

Family History.—This was negative.

Personal History.—Five weeks before admission to the hospital the patient was taken with high fever, headache and prostration. The fever apathy continued for two weeks, during which time the child vomited frequently. The fever then ran a lower course and the child became somewhat brighter, complained of severe headache, vomited occasionally, and was constipated. The patient complained of pain in the right eye and right hand. There had been no convulsions. The child was quiet but the parents thought it did not sleep. There was sighing respiration.

Examination.—When admitted to the hospital: The patient was soporose, although he answered questions. There was slight rigidity of the neck, and a tendency to yawn. There was some hydrocephalus on the right side. The reflexes were exaggerated; the pulse equal, regular, no paralyses noted of any kind. There was slight neck rigidity, *tâche cérébrale,* signs of hydrocephalus on both sides; later on the abdomen was retracted; *left internal strabismus,* patient stuporous but conscious when roused; no evident paralyses. A lumbar puncture yielded 30 c.c. of clear fluid under some pressure. A day subsequent to admission the patient was brighter. An examination of the fundus oculi revealed some small retinal hemorrhages suggesting compression of the cerebral retinal arteries but no choked disk.

Five days after admission patient was conscious with the above ocular palsy, but interested in his surroundings; some exaggeration of the knee-jerk. On walking the patient showed some tremors; complained of headache, was apathetic, pupils uneven, right larger than the left. Four days subsequently he was still apathetic and complained of headache.

A second lumbar puncture four days after the above entry yielded 40 c.c. of clear fluid under some pressure.

Two weeks after admission the patient was still apathetic, soporose, with neck rigidity, and showed slight flatness of the right side of the face.

The eyes examined by Dr. May at this time showed optic nerve atrophy, so-called postneuritic atrophy, with hemorrhage in the retina. The patient was brighter but there was still some neck rigidity and signs of hydrocephalus.

After four weeks the patient was able to be out of bed; there was some mental obtuseness, marked signs of hydrocephalus; no blindness. There was a distinct ataxia or cerebellar gait; mentality continued below the normal. The patient was up and about, without temperature and played with other children.

Puncture fluid examined showed no bacteria; 100 per cent. lymphocytes; some reaction for sugar and albumin.

The von Pirquet tuberculin reaction was negative; blood showed 12,000 leukocytes, with a differential count of 51 per cent. polynuclears on admission. On discharge, or near that, the count was 8,000 leukocytes.

The temperature was normal after the first twenty-four hours' stay in the hospital, with the exception of a rise in temperature, due to an injection of the serum of Flexner as a safeguard, should examination of the fluid show meningococci.

Discussion.—This is a typical case of polioencephalitis resembling very much a tuberculous form of meningitis—the slight rigidity, stupor, hydrocephalus and low leukocyte count. The history, however, showed an acute onset five weeks before admission to the hospital. The puncture fluid also showed fully 100 per cent. of lymphocytes, a fact which might very well be linked with tuberculosis. The child was discharged from the hospital well, however, with the remains of the encephalitis in the form of hydrocephalus and impaired mentality. The only paralysis during the illness was ocular.

Case 2.—J. C., male, aged 7½, was admitted Dec. 22, 1908.

Family History.—Negative; no tuberculosis.

Past History.—None of the exanthemata; was perfectly healthy before the present illness; no pulmonary symptoms; bowels always normal; no urinary symptoms.

Present History.—For the previous two weeks the parents had noticed that the child had not acted as he did previously; he would cry out suddenly and then laugh; was pale; had no fever; no other symptoms until three days prior to admission when he suddenly became stuporous, cried out, complained of headache. Since then the stupor had deepened, the child almost constantly moaning and crying; no convulsions.

He had slight fever, no retraction of head, no photophobia; neck was somewhat stiff; no vomiting; bowels had been obstinately constipated; did not take any nourishment; no twisting of the face, and the child did not move its right arm as well as its left; occasionally cried out at night; with grinding of the teeth.

Physical Examination.—Fairly well nourished, lay in a stuporous condition; head somewhat retracted, patient constantly sighed and moaned with grinding of his teeth; restlessness during examination; seemed unable to move the left arm and leg, respiration was very irregular; practically no rigidity of the neck; some Macewen, especially on right side of the head; *tâche* present; no Kernig, no hyperesthesia, slight photophobia. Mucous membranes normal; no ataxia; no herpes; ears negative; eyes, both upper lids somewhat ptosed, pupils equal, regular, reacted to light; eyes had a slight nystagmus-like motion; no strabismus; conjunctivæ somewhat injected; no petechia; some excoriation about the alæ nasi; teeth and gums in fairly good condition; sordes on lips; tongue coated. Posterior cervical and a few small axillary glands enlarged. Examination otherwise negative; chest fairly well formed; lungs negative; heart normal; action somewhat irregular and rapid; no murmurs; abdomen retracted, lax, no pain; normal; liver normal; spleen negative.

Extremities: Right arm somewhat spastic, hand held clenched, and, as noted above, the child was inclined to move left extremity more than the right; knee-jerks exaggerated. No Babinski, no ankle-clonus.

December 23 lumbar puncture; 33 c.c. of clear fluid under moderate pressure removed; tuberculin cutaneous reaction negative. White blood cells 10,000; 64 per cent. polynuclears.

December 24. General condition somewhat better; less irritable, lay in a semistuporous condition; eyes slightly rotated to the left; no rigidity of neck; no Kernig. Second tuberculin reaction negative.

December 25. Examination of the eyes negative.

December 27. General condition fair; still irritable; did not speak; rigidity of the neck; no signs of hydrocephalus; pupils equal; knee-jerks exaggerated; left tendon reflexes exaggerated; physical condition the same.

December 28. Lumbar puncture; 20 c.c. of clear fluid removed.

January 1. The patient for the previous few days had had periods of stupor and maudlin delirium, in which he cried in a low tone; did not answer questions; did not seem conscious of his surroundings; no paralysis of the extremities, with the exception of the right upper extremity, which seemed to be weaker than its fellow; patient turned his head from side to side constantly; did not take nourishment; no signs of nuclear involvement in the shape of paresis or paralysis.

January 2. Tuberculin reaction negative; general condition much improved; very noisy and delirious most of the day; had a hot bath and then became brighter; seemed to see and hear when spoken to, but did not speak; he motioned with his hands. Very noisy the previous night; took nourishment better; lungs and eyes negative; no paralysis; moved the left arm more than the right; knee-jerks exaggerated.

January 6. The patient in the morning was conscious; sat up in bed with a meaningless smile, when he talked speech was indistinct; had a nasal timbre. Patient did anything he was told to do; had marked loss of power in upper and lower extremities; had a Romberg; when he stood or walked he staggered; his arm and fingers taking on position of athetosis; had no paralysis or paresis of facial muscles; expression of eyes rather vacant, but was conscious and brighter.

January 9. Patient much quieter and brighter, had at times an idiotic smile; speech somewhat indistinct, and had a nasal tone; slight flatness of right side of face; tongue deviated slightly to the right; pupils central—reacted to light; right grip not as strong as left; no apparent atrophy, used arm fairly well; the right leg was quite as strong as the left; knee-jerks active; otherwise negative.

January 16. Discharged well; no paralysis; bright; speech still somewhat nasal.

The temperature the first week, from December 21 to 28, ranged from 98.5 to 99.8 in the rectum. After that it remained normal for four weeks, when he was discharged.

The urine was examined three times during the stay in the hospital and was found negative. The lumbar puncture fluid was examined twice.

January 2, Cytology, 100 per cent., lymphocytes; bacteriology, negative; traces of albumin. The second specimen 50 c.c.; report of sugar reduction; 95 per cent. lymphocytes; mononuclears; no bacteria. Pathologist thought it had more the character of a transudate than an exudate.

Discussion.—In this case there is an imperfect previous history in that no sudden onset with fever was obtained, but there was a period of two weeks of mental irregularities, slight fever and increasing sopor. The patient on admission to the hospital was unconscious and delirious. This delirium was of a distinctly maudlin variety and cleared up completely, leaving a bright intellect. There was on admission, also, rigidity of the neck, vomiting and headache. There was no real paralysis or strabismus. The reflexes were increased. There were signs of internal hydrocephalus. In this case there was a distinct marked leukocytosis, 30,000, with a polynuclear blood-count of 88 per cent. The puncture fluid also showed a lymphocytosis of 100 per cent. and 95 per cent., sterile to culture; some albumin and sugar. There was during the course of the affection slight flatness of one side of the face, some slight deviation of the tongue, and a nasal timbre to the voice. The latter persisted until his discharge.

CASE 3.—J. H., aged 4½, was admitted to the service March 2, 1909.

Family History.—No tuberculosis; the stepmother had a cough and hematemesis and saw the child frequently.

Previous History.—No measles, scarlet fever, pertussis or diphtheria; at the age of 6 months the patient had pneumonia for five days.

Present Illness.—This began five weeks prior to admission with occasional vomiting, which increased in frequency until the child vomited after each meal. No vomiting occurred in the previous two weeks. At that time the child complained of headache and pain in the abdomen, and continued to complain of headache up to admission; had marked cough for a short time two weeks prior to admission and began to be drowsy and slept a good deal of the day; was conscious and recognized mother and asked for food, and played with her toys until five days prior to admission, when she developed rigidity of the neck. For the previous five days the child had seemed to be brighter and had remained in bed, up to that time she was up and about; *she did not seem to see well.* No fever or paralysis; the bowels were constipated; history of low temperature; no febrile movement.

Physical Examination (by house physician).—General condition poor, though fairly well nourished; marked rigidity of neck with Macewen; no Kernig; *tâche cérébrale* present; patient lay in a stuporous condition; could not be roused; made motions with the hands, did not talk; no hyperacusis, no photophobia; somewhat irritable when disturbed; no eruption on the skin; the ears were negative.

Eyes.—Left pupil larger than the right; they reacted to light; conjunctivæ negative; left internal strabismus; no facial paralysis; teeth and gums in fair condition; tongue coated, moist; throat slightly red; larynx, trachea, and thyroids negative; a few axillary glands could be felt; chest fairly well formed; otherwise negative; heart negative; abdomen negative; liver also; spleen not felt; genitals negative, with slight discharge; no edema of the extremities; knee-jerks exaggerated; there was ankle-clonus on both sides; there was a Babinski on left side; no paralyses.

Synopsis.—Stupor, irritability, rigidity, Macewen, *tâche,* ankle-clonus, Babinski, exaggerated knee-jerks, left internal strabismus.

March 3. Lumbar puncture; 30 c.c. of clear fluid containing flocculi was removed. Blood examination: Leukocytes, 30,000, polynuclears 88 per cent. Fundi of eyes examined; negative.

March 5. General condition about the same, patient was in bed; stuporous, but could be roused and then was irritable; moderate retraction of head, marked rigidity of neck, Macewen, slight Kernig; *tâche* present; slight weakness of the left external rectus; no paralysis nor paresis; did not void urine; must be catheterized. Respiration cerebral; no clonus, no Babinski.

March 7. Patient was irritable when disturbed; quiet when left alone; had a Kernig, rigidity of neck, Babinski, no Macewen; cries out. Lumbar puncture; 33 c.c. of clear fluid obtained; contained flocculi.

March 10. Patient was conscious; irritable and disposed to cry; sat up in bed when not watched; noticed everything around the bed. Slight Kernig with Babinski, especially on right side; rigidity of the neck; took nourishment; fundus of the eye normal.

March 12. This a. m. the patient was noisy; had distinct retraction of head; rigidity, Kernig, Babinski, opisthotonos; no paralysis of the facial muscles; took nourishment fairly well; was conscious; pulse slow and regular. White blood cells, 12,200; polynuclears 71 per cent.

March 14. Patient was more rational; sat up in bed; no paralysis; there was slight rigidity of neck, slight Kernig, no Macewen; chest and abdomen negative; took nourishment quite well; tuberculin reaction negative.

March 15. Improvement continued; patient sat up and noticed objects; was less irritable; had slight internal strabismus on the left side.

Patient's general condition was good; was more conscious; more or less aware of surroundings, no rigidity, no Kernig, slight Macewen on left side, no paralysis of limbs. Weakness of the left internal rectus.

March 17. Patient was examined with reference to paralysis; none of the face and extremities was found; strabismus still noted.

March 28. Patient had been up and about the last week; had only a left internal strasbismus left. Discharged.

During the patient's stay in the hospital the temperature ranged from 98 to 100.8 F. in the rectum during the first week, and then fell to normal; pulse and respiration ranged from 20 to 30 for the latter to 90 to 136 for the former, the latter during the fever. When she was up and about the patient's pulse and respiration were 80 and 24 respectively.

The night nurse noted that during the first week the patient slept fairly well, but cried out at night and was restless at times; it was necessary to catheterize the patient; but after March 6 the patient, though restless, slept fairly well without any delirium. The urine examined during the patient's stay in hospital was negative.

The cerebrospinal fluid examined was negative on first puncture as to bacteria; there was a slight amount of albumin present and some sugar.

The second lumbar puncture, March 10, gave a cytology of mononuclears of 98 per cent., with no bacteria to culture or to spread; there was some albumin, 2 mg., and no sugar.

Discussion.—I saw this case in consultation. The onset was more or less acute. The subsequent history resembled a tuberculous meningitis, and the diagnosis was placed as a probable instance of this disease. In the hospital the symptoms cleared up, so that the patient, who was exceedingly bright, was up and about after two weeks. It is to be noted after discharge that though the patient's eyesight was good she returned in a month with a history of blindness of sudden onset. This, after a while, cleared up so that the patient could discern objects clearly. The fundus showed an optic atrophy. In the course of the affection there was a blood leukocytosis of 30,000, with a polynuclear count of 88 per cent. The fluids obtained by lumbar puncture gave a lymphocytic cytology of 98 per cent., some albumin, no sugar. The urine was negative; as also the lungs. Repeated von Pirquet skin tuberculin test was negative, and the temperature for the stay in the hospital did not exceed the normal after the first week. This case so closely resembled a tuberculous meningitis that a differential diagnosis without prolonged observation seemed impossible.

Case 4.—S. F., schoolgirl, aged 11, was admitted to the hospital Feb. 8, 1909.

Family History.—Seven other children living and well. No history of tuberculosis.

Previous History.—Measles, no scarlet fever, no pertussis, no diphtheria, occasionally sore throat, no rheumatism, no pneumonia, no other complaint.

Ten days prior to admission the patient was taken ill and was in bed with high fever, vomiting, headache, malaise; then patient was up and about, but complained of occasional headache until February 7.

Present Illness.—The day before admission she had severe headache, and began to vomit; this continued until the day of admission, when she had general convulsions. Starting with a severe convulsion she had passed into a state of unconsciousness with some fever. The convulsions were repeated and back and neck became rigid; the bowels were constipated; there was no cough or vomiting on day of admission to hospital.

Physical Examination.—(By house physician.)—General condition fair; patient well nourished; slight soporose condition; patient continued to lie on the left side; conscious; irritable; there was some rigidity of the neck; marked Macewen; slight Kernig; *tâche cérébrale.* Patient could be roused from soporose condition; did not seem to be conscious, but simply moaned and cried; respiration somewhat irregular; cheeks flushed; put hands to head at times; twitching;

no retraction of the head. The skin showed some flea-bites, "*tâche bleuatre;*" no petechia; ears and mastoid negative; pupils regular; central, easily dilated; conjunctivæ injected; no paralysis; there was sordes in mouth; teeth and gums in good condition; tongue was coated and moist; throat showed muco-pus; no facial paralysis; thyroids and spine negative; few small axillary and inguinal glands to be felt; chest negative; somewhat sunken; abdomen retracted; liver, spleen and genitals negative. Extremities: Slight edema over the tibias; knee-jerks not obtained; no Babinski; no paralyses.

Synopsis.—Stupor, Macewen, Kernig, rigidity of the neck, *tâche cérébrale.*

February 9. Lumbar puncture; 35 c.c. of clear fluid removed under great pressure, and 30 c.c. of Flexner serum injected as a precaution should meningococcus be present on examination. White blood cells, 72,000; polynuclears, 79 per cent. Cutaneous tuberculin reaction negative.

February 10. Patient lay in a crouched position; was irritable when disturbed; cried out and was exceedingly hyperesthetic; retraction of head, rigidity, Kernig, as on the previous day; arms and extremities showed some edema still present; patient had ordinary redness of fauces; chest negative; patient did not take nourishment.

February 11. Patient had a general exanthematous rash (serum); patient lies in same position as on the previous day; general condition about the same; delirious when disturbed; rigidity and Kernig still present. Nurse reported that patient sat up and took notice of things.

February 12. The patient was much improved; opened her eyes and seemed to notice objects; was much clearer and did not resist quite so much. There was still very marked Kernig and very marked rigidity of the neck and retraction of head; there was also mydriasis when the head was flexed and slight strabismus on the left side.

February 13. When the patient was admitted the urine was of a distinctly brownish tint; it had now become clear but was distinctly colored; estimate of urine very difficult on account of the involuntary discharges; patient when left alone was very quiet; when interfered with still resisted; did not answer questions. Patient seemed to be more conscious, but was apparently deaf; no paralyses; Kernig still present.

White blood cells, 12,000; polynuclears, 83 per cent; fundus of the eyes normal.

February 14. Patient the previous night sat up; was quite logical, but apparently deaf; when any one came near her the patient was frightened, but was more rational than the previous day; no edema of the tibia. There was a Kernig, rigidity of the neck, no Macewen, excretions involuntary.

February 15. Patient could hear; was more rational; had external strabismus of right eye; this was noted the previous day; rigidity of neck still present; as also Kernig; had normal reflexes on both sides; some edema of the tibia.

February 16. Patient improved; more rational; Kernig and rigidity still present; the urine was normal.

February 17. Patient sat up; was quite rational; external strabismus of the right eye unchanged; Kernig still present; headache of the day before was gone.

February 19. The patient continued to improve; no apparent paralyses of the extremities; no paralysis of facial muscles.

February 22. The patient complained of lack of power of left hand; right grasp a little stronger; no limitation of motion of upper extremities; no apparent atrophy.

February 24. Slight limp in left leg, knee-jerks on left side diminished.

February 25. Patient looked bright; felt well; slight Kernig; slight weakness of left upper extremity.

March 2. Patient examined to-day; appeared bright and normal; slight loss of power in left hand; no atrophy of muscles visible in upper and lower extremities; no loss of power; no Kernig; no Babinski; no ocular or facial paralyses. Patient had loss of power in left arm, but this was more apparent than real.

The temperature of the patient, which from admission February 8 to February 14 ranged up to 104 F., gradually fell on February 14 to 100 F.; respiration became pretty regular—from 22 to 32—and the pulse was 90 to 120. The following day the temperature, pulse and respiration were normal.

The night nurse reported that on admission and at intervals afterward the child was particularly noisy at night. During the day she was quite comfortable. The urination was almost always involuntary. She refused nourishment, was constipated up to February 12, after which time she slept at night and was quiet. The puncture fluid was reported as practically normal; there was sugar present, also traces of albumin; cytologic examination showed a few mononuclear cells. Wassermann was negative. The urine was obtained by catheter and, with the exception of a few bacterial cells, was sterile.

Examination of Urine.—February 11, hyaline and granular casts, and some blood and pus were present. February 12, about the same—blood, pus and casts. February 14, a few granular casts. February 15, no casts and no blood; negative after that time with the exception of a few leukocytes.

Discussion.—In this case the onset was acute, there then was a remission in symptoms and then the patient took to bed after a week with all the symptoms of a meningitic attack; in fact, when seen in consultation a cerebrospinal meningitis was suspected, and a puncture was made with that diagnosis in view, but the fluid obtained was clear and nothing found but a lymphocytic cytology. There was a high leukocyte count of the blood, including an excess of polynuclear cells. The illness ran the course of an acute meningitis. The finding in the urine corresponds to that of Wickman in one of his cases. Inasmuch as the urine cleared up completely, it must be surmised that the nephritis was only part of a general infection. The patient fully recovered, with a strabismus due to ocular palsy remaining with slight weakness in the left upper extremity. This, I think, is a case of acute polio-encephalitis with a meningitic onset, its course closely simulating cerebrospinal meningitis of the epidemic type. The patient was not discharged until she had absolutely recovered.

CASE 5.—Female, aged 5, was admitted Oct. 14, 1909.

Family History.—Father suffered from pulmonary tuberculosis; mother and nine other children healthy.

Previous History.—The patient was born at full term; no instruments used; measles at 2½ years; no complications; whooping-cough just previous to measles. The patient had a moderate dry cough since having measles up to one year prior to admission. No convulsions, no ear symptoms, bowels regular, urination normal. About sixteen months before admission the patient was operated on for acute appendicitis; ill five weeks; healthy since until present illness.

Present Illness.—Present illness began four days prior to admission, when the mother noticed that the child became drowsy, lost interest in her surroundings and developed moderate fever. The next day the child vomited for the first time. The vomitus consisted at first of undigested food; later of small amounts of bile-stained fluid, accompanied by much retching; vomited since, chiefly after taking food.

Since the onset the bowels were obstinately costive; no marked abdominal distension, no blood or mucus in stool. Drowsiness became intensified; child would start in her sleep with a shriek; sighed considerably. The day before admission the child complained of pain in back of neck, developed some rigidity and became delirious and irrational; no convulsions, no palsies, slight dry cough, no dyspnea; marked prostation; drowsy; responded when disturbed; was irrational and delirious; respiration irregular; no head retraction; neck was rigid; general hyperesthesia; Macewen present, especially on left side; marked photophobia. Eyes, ears and mastoids normal; skin showed scar of operation; *tâche cérébrale* present; scattered papular spots; a few small lymph-nodes in left axilla; tongue, dry and coated; throat, teeth and gums in good condition; chest well formed; lungs clear; heart borders normal; action regular, rapid, of poor force, sounds clear, no murmurs; pulses equal, regular, rapid, small.

Liver and spleen not enlarged; abdomen lax; reflexes present.

Extremities.—Kernig's sign present on left side; left, Babinski at times.

Synopsis.—Fever, drowsiness, delirium, hyperesthesia, rigidity of neck, Macewen, left Kernig.

Blood Count.—White blood cells, 21,000; polynuclears 61 per cent.; small lymphocytes 28 per cent.; large lymphocytes 11 per cent.

October 15. Lumbar puncture; 24 c.c. clear, colorless fluid under increased tension withdrawn.

October 16. This morning patient was semiconscious; roused when talked to; athetosis in hand; dry, coated tongue; talks with lisp; slight flatness of left side of face; Kernig on both sides; marked rigidity and tenderness of neck; slight Macewen on left side.

October 17. Lungs negative; paresis of left side of face more marked; marked rigidity of neck; marked Kernig on both sides; fundus examination of eyes was negative; patient semiconscious. Von Pirquet positive.

October 18. More conscious; Kernig; Macewen very slight on left side; slight internal rotation of left eye; marked neck rigidity.

October 23. Von Pirquet still evident; Kernig, left facial flatness; bromic eruption on legs; could sit up; rigidity of neck almost gone; tongue moist; Macewen not elicited.

October 25. Sat up; left side of face still slightly flat; neck supple; Kernig, 30 degrees on both sides.

October 24. Urine amber, acid, specific gravity 12, albumin 0; a few white blood cells.

November 4. Urine amber, acid, specific gravity 24, albumin 0; a few white blood cells.

October 15. Cerebrospinal fluid showed lymphocytes 100 per cent.; negative for bacteria; no growths; no tuberculosis; albumin .5 mm.; sugar reducing substance present; Widal negative 1 to 20, 1 to 50; also on October 18.

October 14. Temperature 104.2 F. on admission; dropped to 100.8 F. on following day; and on sixteenth reached 99 F.; slight rises to 100 F. afterward. Pulse 116 on admission, respiration 28. Weight 45¾ pounds.

Discussion.—This patient, 5 years of age, was attacked more or less acutely with high fever and vomiting, passed into a condition of sopor which became intensified after a few days. There was the picture of meningitis with fever, drowsiness, delirium, apathy, vomiting, constipation, pain in neck and rigidity of the neck. What was especially disquieting was a positive von Pirquet cutaneous reaction to tuberculin, which misled into the diagnosis of tuberculous meningitis. The subsequent complete recovery disproved this, leaving us to infer a latent glandular tuberculosis. The fluid obtained by lumbar puncture showed nothing more than a marked lymphocytosis.

The recovery of this patient was complete, there being left only a slight facial flatness; no real paralysis. The temperature after the first day following admission to the hospital was normal; the urine was normal; the fundus oculi was normal.

Case 6.—This case resembles a case I saw recently in consultation, a girl of 13. The girl was seen by several physicians, all being quite positive in the diagnosis of tuberculous meningitis. This girl like the case I am to depict recovered, with the exception that she did not, as in this case, yield a positive tuberculin reaction.

History.—The patient was a boy, aged 4, admitted to my hospital service. He had had measles, scarlet fever and diphtheria.

Present Illness.—This began three weeks before with an attack of fever and vomiting and headache; following this the boy became drowsy, did not notice and was soporose and stupid. The condition of drowsiness became more and more marked, and in this condition he was brought to the hospital. The patient was well nourished, had some slight hydrocephalus, staggered when upright, swayed especially to the left when he walked and threatened to fall. The patient was in a trance-like state and sat up in bed staring ahead; he slept well. The examination of the fundus oculi was negative.

The patient's urine at first contained acetone, diacetic acid and a trace of sugar. These disappeared in the first two days of the hospital stay. After three weeks of illness the above symptoms cleared and the patient was well. There was from the first a positive tuberculin skin reaction (von Pirquet). No lumbar puncture was made. This case differs from that of the girl I just mentioned, inasmuch as the latter had no tuberculin reaction and was unable to sit up or stand without experiencing marked vertigo. The girl was highly hyperesthetic, whereas this symptom was absent in the boy.

Case 7.—C. R., aged 5½, was admitted Jan. 10, 1911.

Family History.—Negative.

Previous History.—Had pneumonia and measles one year ago; no other diseases. The child was perfectly well until thirteen days before admission.

Present Illness.—This began thirteen days previously with vomiting and headache. The child vomited one to three times practically every day since onset; vomiting was not projectile in character, having no relation to meals. Headache had been frontal in location and almost constant in character; had slight fever following the onset; for a week had occasional cough, with slight mucopurulent expectorations. For two days the father noticed that the child had been drowsy most of the time, and was rather irritable when awakened. There were no disturbances of the special senses; no paralyses noted; no ear disturbances; bowels fairly regular; urination normal; appetite poor; no symptoms of cardiac or renal disturbances.

Synopsis.—Vomiting and headache for three days, slight fever, slight cough; drowsiness for two days.

Physical Examination.—General condition good; well nourished; irritable. Head—no rigidity, no Macewen. Eyes—pupils equal; react to light and dilate, no palsies. Ears and mastoid negative. Mouth and teeth—several upper teeth missing; otherwise in fair condition; tongue moist and coated; throat congested. Glands and skin negative; chest well formed, expansion good; lungs negative; heart, regular, good force, no murmurs; liver—fifth space, sixth rib to free border; not felt; spleen not felt. Abdomen held tense; tympanitic; no masses; abdominal reflexes not obtained; slight *tâche.*

Extremities.—Knee-jerks much exaggerated; no Kernig, no clonus; Babinski and Oppenheim, bilateral; patella-jerk bilateral; tremor of upper extremities.

Genitals.—Some reddening of vulva; no discharge. Rectal examination not made.

Synopsis.—Irritability, exaggerated knee-jerks, Babinski, Oppenheim, tremor of upper extremities.

January 11. White blood cells 31,200; polynuclears 80 per cent.; lymphocytes 18 per cent.; large mononuclears 1 per cent; basophils 1 per cent.

January 12. Ears negative. Lumbar puncture made; about 30 c.c. of clear fluid and flakes withdrawn.

January 13. White blood cells 21,200; polynuclears 80 per cent.; lymphocytes 14 per cent.; large mononuclears 5 per cent; easinophils 1 per cent.

January 16. General condition better; child brighter; slight rigidity of neck persists; no Kernig.

January 22. Inner reflexes present; child will not stand; eyes closed; uncertain gait present.

January 24. Child had been picking up but complained of pain in extremities; reflexes increased; Kernig present; resents interference; no pain in back; no headache.

White blood cells 10,600; polynuclears 73 per cent; small mononuclears 26 per cent.; large mononuclears 1 per cent.

February 7. Patient up and about ward.

The temperature during the first week of the hospital stay ranged from 99 to 101 F. and then dropped to the normal.

Urine during stay in hospital at only one time showed a few hyalin casts.

The fluid obtained by lumbar puncture contained 90 per cent. lymphocytes and 10 per cent. polynuclear cells. Smears and culture negative as to bacteria; sugar, moderate reduction; some albumin.

Discussion.—The onset was sudden, with headache and vomiting daily, slight fever with cough, and after ten days, increasing sopor and irritability. On admission to the hospital there were no palsies, but there was the mental irritability, exaggerated reflexes with tremors of the extremities. The blood showed during the illness a marked polynuclear leukocytosis with a lymphocytic picture in the spinal puncture fluid.

I have thus described a condition which is of great interest. It is apt to be, and is constantly, mistaken for meningitis of the cerebrospinal, acute suppurative or subacute tuberculous form. The onset of the illness is acute; it begins with a previous history of absolute health. After the acute symptoms set in there may be in some cases an abatement and then a recurrence of symptoms of a cerebral nature, which gradually deepen. If the case is one resembling an acute meningitis, the symptoms are more active, with neck rigidity, pain in the neck, headache and delirium. If the case resembles the tuberculous form of meningitis, the patient lies more quietly, exhibits palsies of the cranial nerves, and may even have marked hydrocephalus with distinct Cheyne-Stokes respiration and unconsciousness. In both sets of cases the delirium, sopor or coma lightens, the patients after a week or more of illness become brighter, and recovery proceeds. Lumbar puncture in all the cases reveals a clear or slightly flocculent fluid, without bacteria, and a cytology of 90 per cent. to 100 per cent. lymphocytes. An examination of the blood shows at first a leukocytosis of pronounced degree of the polynuclear type.

The onset of the disease may be ushered in by fever, which rapidly subsides to within a fraction of a degree of the normal and the major part of the illness runs its course with this temperature, which is practically normal. The diagnosis is made from the points of clinical course laid down in this paper. The prognosis is for the most part good, except in those cases which involve the nuclei of the nerves controlling respiration. In such cases the outlook is that of an acute bulbar paralysis, when the extent of the lesion will decide the fate of the case. The main point is to have in mind the great similarity of a certain set of these cases to those of tuberculous meningitis, and acute cerebrospinal meningitis, and the absolute futility of a positive diagnosis without study of the case, lumbar puncture and all the clinical aids at our command.

The fatal cases of the cerebral forms of polioencephalitis have been mentioned in this paper. I have two cases of this kind to report, in one of which autopsy was performed and the diagnosis of polioencephalitis confirmed. These cases may be of sudden onset with cerebral symptoms, and a rapid involvement of the bulbar nuclei. The result is a picture of acute bulbar paralysis with cerebral onset. In some cases the onset may be gradual, in others acute. The paralysis involves the muscles of deglutition and phonation and this is the first sign of bulbar involvement of a serious nature. In these cases the ocular and facial nuclei may be involved, and as the process spreads down there is a complete paralysis of a descending type, involving the muscles of respiration. In one of the cases the respirations seemed to cease first while the heart continued beating. All cases here recorded were fatal cases, but this must in no way be assumed to be always the case, because I have seen a few bulbar cases recover, one notably in a child 3 years of age, in which the respiration was involved, as was also deglutition. In this case a complete recovery occurred.

Case 8.—A. B., male, aged 5, was admitted Oct. 4, 1908.

Family History.—Father had tuberculosis in 1905 when at Bedford Station; since then was well. He had lost 5 pounds in the previous few weeks. The mother and two other children were well.

Previous History.—The patient had measles two years ago; otherwise no illnesses; bowels always regular; appetite good; mentally bright; never complained of headache; eyes and ears good; no eruptions on skin.

Present Illness.—Onset one and one-half weeks prior to admission, with indefinite symptoms. It was noted that the child was weak and lackadaisical; did not complain of headache; had no convulsion or palsies; had some fever; appetite was good; child slept uneasily at night and cried out in sleep; bowels regular; in the previous four days the child began to cough when talking; had difficulty in swallowing; regurgitation and coughing back food mixed with mucus; had been unable to talk in this time; unable to sit up or walk; ears and eyes remain functionally unaffected; complained of slight pain over heart; cried out frequently in sleep and had involuntary movements of arm.

Physical Examination.—General condition fair; patient well nourished; lay in an apathetic condition; cheeks flushed; moderate dyspnea; child was hoarse; marked gurgling in throat; alæ nasi dilate with each inspiration; child responds when spoken to; voice thick and husky; moderate rigidity of neck; on bending neck child was irritated; Macewen on left side; no irregularity of skull; no definite tenderness made out; no retraction of head; child somewhat irritable; Kernig; *tâche cérébrale* present; moves arms and lower extremities, but acts as if in trance; answers monosyllabic.

Skin and mucous membranes had a good color; ears and mastoids externally negative; moderate amount of cerumen in canal; eyes and upper lids somewhat closed so that upper one-half of pupil was covered. This could be overcome and child raised lid in normal manner. Pupils: right slightly larger than left, regular, central moderately dilated; reacted somewhat sluggishly to light and accommodation; weakness of both external recti; conjunctivæ negative. Nose—evidences of slight secretion ali nasi; otherwise negative. Face—left-sided facial paresis. Mouth, teeth and gums in poor condition; tongue thickly coated and moist; tonsils hypertrophied. Throat—uvula elongated; throat slightly ingested; palate moves slightly. Larynx, trachea, thyroid, spine, bones and joints negative; a few small cervical and inguinal glands were palpable.

Chest was well formed and symmetrical; right chest seemed to expand slightly more than left; no retraction.

Lungs: Anteriorly there was some dulness over the right axilla; marked bronchial râles over entire chest; breathing over anterior chest was exaggerated; numerous loud gurgling râles and expirations which seem to be transmitted from trachea. In the right axilla there were a few mucus râles on inspiration; posteriorly there was dulness at right apex down to about two fingers below spine; dulness at left apex of similar extent; over entire chest posteriorly there were numerous bubbling râles on inspiration and expiration; most marked at left base; breathing harsh and exaggerated; no change in voice.

Heart: Right border at right border of sternum; left border in nipple line; visible beat at fourth rib; apex neither seen nor felt; sounds clear; no murmurs; action regular; good force; somewhat accelerated.

Abdomen: Somewhat retracted and lax; no pain or tenderness. Liver, fifth rib to sixth rib; free border not felt; spleen not felt.

Extremities: Upper, grips seem to be equal; child seems to use left hand more than right, although both can be used fairly well; right arm weaker than left; no impairment on passive motion; no atrophies; arm reflexes present. Lower slight edema; knee-jerk not obtained; no clonus; no Babinski; no paresis or paralysis of legs.

Genitals: Double cryptorchidism. Rectal examination not made.

Blood: Leukocytes 25,000.

October 15. Eyes examined and found negative.

The child's condition remained about the same; lay quietly, preferably on the right side; child gets frequent attacks of dyspnea, which were accompanied by loud breathing; on auscultation there were found numerous moist gurgling râles throughout the chest; child takes nourishment very poorly, owing to the difficulty which it has in swallowing; reflexes in extremities gone.

October 16. Condition remained the same; lay quietly; eyes half open; had some photophobia and could see objects readily; had slight weakness of the external and internal recti muscles of the eyes; could not swallow; regurgitated all food given by gavage; breathing remained the same; signs of pulmonary edema came on frequently and cleared up in a large measure after hyperdermic injection of atropin. It was necessary to resort to rectal feeding. Lower extremities had no reflexes; abdominal reflexes also gone; there was no Kernig; electrical reactions and sensations not yet tested.

Blood: Leukocytes 33,000.

Urine: Hyalin casts; few granular casts.

The patient died with signs of respiratory failure. Postmortem made.

CASE 9.—G. R., female, admitted November 4, 1910.

Family History.—Seven other children, all well; father coughs; no tuberculosis.

Previous History.—The patient had measles; no other disease; no cardiac, pulmonary or renal disease, no rheumatism. Previous to present illness the child was perfectly well and played about in the street.

Present History.—At 5 o'clock a. m. on the morning of admission the child had involuntary urination while in bed; on taking her up she squirmed about and screamed; it was then noticed that the child could not articulate and could not stand on its feet; vomited once in the morning, and whenever she was given anything to eat; appeared to have some difficulty in swallowing; all day the child lay quietly in bed without moving a limb; had no fever.

Physical Examination.—General condition good; patient well nourished; flushed facies; markedly apathetic; somewhat stuporose; respiration somewhat rapid and regular; does not cry nor give response to spoken language; neck, no rigidity, no mastoid; Macewen present; distinct flatness of right side of face; right palpebral fissure not completely closed; mouth drawn to the left.

Eyes: Pupils equal, central and regular; mucoid discharge from conjunctivæ; no corneal anesthesia; no petechia or palsies; dry crusting of nose; lips of good color; tongue somewhat coated; gums in good conditions; teeth in good condition; pharynx negative; palate, slight deviation to left; moves actively; skin, clear, good color; one or two small healing scars.

Glands: Submaxillary, post cervical, chains.

Chest: Well shaped; lungs, negative; heart, borders not enlarged; apex, fourth space within nipple line; action rapid and regular; pulse, equal, regular, rapid.

Abdomen: Negative; liver, fourth to sixth ribs; spleen not felt.

General: Patient unable to hold back up; head falls weakly to side; weakness of right side of body complete; right arm useless; left knee-jerk just present; left arm tendon reflex exaggerated; right knee reflex elicited with difficulty; right arm completely relaxed; apparently no power; slight redness of vulva.

November 6. Patient in a condition of apathy; the Macewen still quite marked, more so than the previous day; right facial paralysis marked; a little weakness of external rectus of right side; complete right hemiplegia; knee-jerks absent on paralyzed side; present on left side; considerable atrophy of the right deltoid, biceps and triceps; sighing respiration; *reaction of von Pirquet 2 mm. positive;* slow, forcible heart action; child vomited once; constipation present; swallowed with difficulty; refused nourishment; did not talk; a little lagophthalmus of right eye.

November 4. Von Pirquet; white blood cells 17,600; polynuclears 82 per cent.; small lymphocytes 16 per cent.; small mononuclears 2 per cent.

There was a slight difference in size of the thighs, the affected being smaller; exaggerated reflex of left affected extremity; only occasionally obtainable on right side; weakness of the muscles of the neck; head fell back; child could sit up.

November 6. Right knee-jerk this morning easily obtainable; left knee-jerk elicited with difficulty; left triceps-jerk exaggerated; right not obtained.

November 7. Heart continued beating after respiration ceased. Temperature ranged from 100 to 104.8 F.; at death 102.5 F.; pulse 96 to 130; respiration 24 to 36.

Fluid obtained by lumbar puncture: First puncture had lymphocytes too few to count; no bacteria; animal inoculated. Second puncture: Cytology, 72 per cent. lymphocytes, polynuclears 28 per cent.; negative to bacteria; albumin 1 mm.; sugar, slight reduction.

Blood culture, negative.

30 East Sixty-Second Street.

INFANTILE PARALYSIS: SPINAL FORM *

JOHN LOVETT MORSE, A.M., M.D.

It hardly seems necessary to consider in detail the symptomatology of the ordinary classical type of the spinal form of infantile paralysis. Everyone knows how varied the onset may be and how much difference there is in the severity of the constitutional symptoms. It is common knowledge that the paralysis comes on quickly in the course of a few hours, or at most in three or four days; that there is then a stationary period of from one to four weeks, which is followed by a period of improvement lasting from six months to perhaps a year, and that the final paralysis is always less than the initial. The improvement in the paralysis is due to the facts that many of the ganglion cells, which at the height of the disease are merely compressed or only partially involved, recover their function, wholly or in part, and that the nerve-supply of a muscle never arises from a single segment of the cord.

It is impossible, therefore, in the acute stage to prophesy how extensive the final paralysis will be. Recovery is sometimes nearly or quite complete when the initial paralysis is very marked, while at other times there is very little improvement, even when the original paralysis is slight. On general principles, however, the greater the extent of the initial paralysis, the later the beginning of the stage of retrogression and the slower its progress, the greater is the final paralysis.

The final paralysis is, as a rule, monoplegic or hemiplegic, seldom diplegic or paraplegic. It seems idle, however, to give statistics as to the relative frequency with which the different extremities are involved or to detail the possible combinations, because these facts are of no practical importance in the individual instance. It is comparatively unusual, however, to have all the muscles of an extremity involved or, at any rate, involved to the same extent. In most instances some of the muscles are spared and in many only one or two are affected. The grouping of the paralyzed muscles has, moreover, no relation to their physiologic function, the distribution of the paralysis in many instances appearing most peculiar. The peculiar distribution of the paralysis is easily understood, however, when it is remembered that the nerve-supply of a given portion of an extremity, the forearm, for example, does not all arise at the same level of the cord, that the blood-supply of the cord is horizontal, not vertical, and that the affection of the cord is due to interference with the

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* Read at the meeting of the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

blood-supply, resulting from inflammatory processes in the vessel walls, due to infection originating in the subarachnoid space.

It is not very unusual for other muscles than those of the extremities to be involved, while these escape. Such muscles are most often the erectors of the spine and the abdominal muscles. The involvement is, moreover, not infrequently unilateral. The paralysis is, for example, sometimes limited to the extensor muscles of the neck, to the muscles of one side of the spine, or to those of one side of the abdomen. Paralysis or paresis of these muscles is often overlooked and the deformities to which they give rise attributed to other causes. Scoliosis from this cause is very often misinterpreted and enlargement of the abdomen from paralysis of the abdominal muscles is attributed to indigestion with flatulence, or to ascites. In one patient whom I saw, a unilateral paralysis of the abdominal muscles had been mistaken for an abdominal tumor. Incidentally, the prognosis in paralysis of the abdominal muscles is fairly good.

THE PROGRESSIVE TYPE

In a certain number of instances the paralysis is of the progressive type. It usually begins in the lower extremities and gradually extends upward, resembling in its course that of the so-called "Landry's paralysis." It is probable, in fact, that a very considerable proportion, if not all, of the cases which have in the past been described under this name were really cases of infantile paralysis. When the paralysis reaches the external muscles of respiration, as it not infrequently does in this type, a fatal outcome is practically inevitable. In certain cases the phrenic nerve is also involved. Death occurs sooner, of course, when this happens. This form must not be confused with that in which death results from respiratory paralysis due to the involvement of the centers of respiration in the medulla. In other instances the paralysis begins in the arms and extends both downward to the lower extremities and upward to the centers in the medulla.

THE POLYNEURITIC TYPE

Pain is a prominent symptom in many instances. It is, in fact, so common that it is hard to understand how the old dictum that there is no pain in infantile paralysis ever originated. The pain is sometimes in the joints, but more often along nerve-trunks, or is indefinite in its distribution. It is usually most marked in the paralyzed parts. There is occasionally tenderness over the nerve-trunks. Pain and tenderness are at times marked enough to cause the paralysis to be entirely overlooked and a diagnosis of rheumatism or scurvy to be made. The extremities are often held rigidly and all motions as vigorously resisted as possible because of the pain on motion. This combination of rigidity and resistance is possible, of course, only when the muscles are but partially paralyzed or when some of them are intact. The failure to appreciate the significance of this condition of combined flaccidity and spasticity has led, in my experience, to many errors in diagnosis during the acute stage. In one of my own cases it was necessary, on account of the rigidity of the leg and the pain which attempted motion caused, to give ether enough to dull sensation before it could be determined whether the trouble was an infantile paralysis or a disease of the hip joint. When pain was no longer felt the affected extremity was flaccid while the muscular tone was normal in the rest of the body.

ABORTIVE TYPE

There is no doubt that the disease occurs very frequently without the development of any paralysis. The term "abortive" ought strictly, of course, to be limited to the cases in which there is no paralysis. There is, however, another class of cases, in which the paralysis is very slight and lasts but a few hours or days, which is on the border-line between the abortive type and the ordinary spinal type. These cases are very easily overlooked clinically unless the symptoms are very carefully studied.

DIAGNOSIS

The diagnosis of infantile paralysis of the spinal type after the development of the paralysis is, of course, very easy. The great difficulty at present lies in making the diagnosis before the appearance of the paralysis. Sweating, marked nervous irritability and hyperesthesia are present in many instances before the onset of the paralysis, but they are not at all constant. If they are present, they are strong evidence in favor of infantile paralysis, but their absence does not count against it. Hyperesthesia is the most constant and the most important symptom of the three.

Although leukopenia occurs in animals during the early part of the acute stage of infantile paralysis, it is certainly not a constant symptom in man and in many instances is replaced by a hyperleukocytosis. Further experience is necessary to determine of how much value the leukocyte count is in the early diagnosis of infantile paralysis. At present it is of little or no assistance. While it is possible that there is a lymphocytosis in the early stages of infantile paralysis, there is at present not sufficient evidence to show whether either a relative or an absolute lymphocytosis is at all a constant phenomenon. If further investigation shows that it is, it should be of considerable assistance in the early diagnosis.

Experimentally, there is an increase in the number of cells in the cerebrospinal fluid during the prodromal stage before the appearance of the paralysis. The polynuclear cells at this time exceed the mononuclear. After the appearance of the paralysis the mononuclear cells quickly out-number the polynuclear. A fibrin clot is often formed in the prodromal or early part of the acute stage. Frissell, in the only instance in which lumbar puncture has been done in man during the preparalytic stage, obtained a slightly opalescent fluid which gave a marked protein reaction with Noguchi's test and showed an excess of polynuclear cells. The formula had begun to change to the lymphocytic, however, before the paralysis developed. Lumbar puncture ought, therefore, to provide a most valuable means of diagnosis in this disease during the preparalytic stage. Its value is considerably limited, however, by the fact that there is nothing whatever characteristic about the early symptoms of infantile paralysis, and, therefore, nothing to definitely suggest its use. In order to recognize the disease early, therefore, before the onset of the paralysis, it would be necessary to do a lumbar puncture on every sick child, which hardly seems a rational procedure.

During the acute stage of infantile paralysis the cerebrospinal fluid is clear, not infrequently under somewhat increased pressure, often forms a fibrin clot on standing, and always contains an excess of cells. These are chiefly of the mononuclear type, most of them being lymphocytes. These changes are, however, identical with those found in tuberculous meningitis, the disease with which it is most likely to be confounded. An increased protein content is also found by the Noguchi test in both diseases. A positive diagnosis between them can only be made, therefore, by the examination of the cerebrospinal fluid for tubercle bacilli. These can be found in the great majority of the cases of tuberculous meningitis if the examination is careful enough. They are more than likely to be missed, however, in the ordinary routine examination. The characteristics of the cerebrospinal fluid in infantile paralysis are, of course, so different from those in meningococcal, influenzal and pneumococcal meningitis that no confusion with these conditions is possible.

The only possible method of making the diagnosis of infantile paralysis of the spinal form before the onset of the paralysis is, therefore, by lumbar puncture. In order to be of much assistance, however, this must be done very generally in sick children during the summer months, because there is nothing characteristic and usually nothing even suggestive about the early symptoms.

70 Bay State Road.

THE CONTROL OF EPIDEMIC POLIOMYELITIS *

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Epidemic poliomyelitis has, since its appearance in 1907-08 along the Atlantic seaboard, extended over the entire United States. This wide distribution has fortunately not been attended by a regular and uniform prevalence of the disease in all communities. Indeed, considerable territories would seem to have escaped its ravages, although few, if any, of the states have remained entirely free from invasion. The number of persons attacked can be only conjectured, but it is probable that it reaches into the thousands. The mortality has been the average noted in the European epidemics, and has approached 10 per cent. Undoubtedly the mild or abortive forms of the disease have prevailed along with the severer paralytic types, and in many instances their nature has been certainly overlooked. Among the paralytic cases all grades of the affection have been encountered, and the number of cases in which complete recovery without residual paralysis has taken place would appear to have been not inconsiderable. In other words, the American epidemic of poliomyelitis is in agreement with the earlier European epidemics in all essential respects, and differs from them only by reason of its wide distribution and great total number of cases. This variation is to be explained probably not by supposing that the conditions for the prevalence of the disease in the United States were more favorable than in Europe, but because of the greater extent of territory embraced under one government. Possibly also the United States have suffered disproportionately and more severely than European countries because of the failure, in many communities, to make prompt recognition of the nature of the malady, and because of the want of a body of authoritative sanitary regulations that could be put into rapid operation in the effort to delimit the spread of the disease through the employment of methods of quarantine. I am convinced that the disease in some communities was mistaken for periods of many months for epidemic meningitis, a fact not highly surprising in view of the lack of general knowledge regarding epidemic poliomyelitis that existed throughout the country, and in view of the common occurrence of marked symptoms referable to meningeal irritation in the course of the malady.

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*From the Laboratories of the Rockefeller Institute for Medical Research.

*Based on remarks made before the Association of American Physicians at Atlantic City, May 9, and the American Pediatric Society at Lake Mohonk, New York, June 1, 1911.

The question of the control of epidemic poliomyelitis is one of high interest at the present time. This control may be of two kinds, namely, that effected through the employment of measures of prevention, and that through the employment of modes of treatment. Of the two possible means of control, the first, that through prevention, is to be given the place of prime importance, for it is not only more humane and scientific to prevent a disease rather than to effect its cure, but in the present instance the knowledge available makes prevention a possible achievement, while there exists no known means of therapeutic control worthy the name.

The measures of prevention employed should be those based on knowledge of the mode of infection that clinical observation and experimental investigation have thus far supplied. At any given period we can apply intelligently and with confidence only those preventive measures that are founded on such knowledge. It would seem to be established that the human agency of transfer of the infectious agent does occur and perhaps frequently. Moreover, this human agency includes not only the actively infected or ill, but also healthy persons who perform the part of intermediaries between the stricken and the well who are to develop the disease. To express this point in somewhat more technical language, we must accept for the present the existence of both active and passive carriers of the infectious agent of epidemic poliomyelitis and accord to each a share in the distribution of the agent through the implantation on other susceptible persons. Hence, in the effort to control this distribution, there should be employed adequate measures of isolation and quarantine of the sick as well as those in immediate attendance on the sick.

We are not sufficiently accurately informed of the period of survival of the infectious agent within the active and passive carriers to enable us to state precisely what the period of quarantine should be. We possess some data, not, however, overaccurate and convincing, based on the period of development of secondary cases of the disease, that suggest that the virus may persist in the infected in an active state for several weeks, and we further possess experimental evidence to the effect that in inoculated monkeys the virus may survive in the mucosa of the nasopharynx at least for several weeks and even several months (Osgood and Lucas, Flexner and Clark). This long period of survival in the monkey would, however, appear to be exceptional. In many instances the virus cannot be discovered in the mucosa as early as one, two or three weeks after the appearance of the paralysis (Flexner and Clark). I am disposed, therefore, to view the examples of long persistence of the active virus in the monkey, with which, doubtless, corresponding examples among human beings will be found, as the equivalent of the chronic carriers of bacteria among men and animals in other well-established types of infectious diseases. Such chronic carriers constitute not only and fortunately an exceptional class, but in framing our practical measures of prevention we have considered them, up to the present time, in rather an incidental way. Thus, for the present it would seem that a period of isolation of from three to four weeks would be sufficient in ordinary cases of epidemic poliomyelitis, it being understood that when the acute or febrile course of a case of the disease is prolonged, the period of isolation be lengthened accordingly.

The efficiency of any group of preventive measures will depend on the directness with which they deal with the source of the infectious agent that they seek to restrain. We have progressed very far into the management of an infectious disease when we have learned the portals of egress and of ingress of the infectious agent. Such knowledge of this kind as we possess regarding epidemic poliomyelitis is based wholly on animal experiments, and hence the degree of its application to human beings has still to be established.[1] It has been shown that in the monkey the virus of poliomyelitis passes from the central nervous system into the nasal mucosa, and it has been found that monkeys can be infected more readily by applying the virus to the nasal mucosa than by any other means except direct intracerebral inoculation. It is for this reason that I believe special attention should be accorded the nasal and buccal secretions of persons affected with epidemic poliomyelitis during the period of isolation, and even for a period afterward. The facts known concerning the relation of the nasal mucosa to the virus of poliomyelitis must be taken at precisely their true value, and must not be considered to exclude other modes of infection by way of other channels in human beings. Hence beside the attention given to the destruction of the nasal and buccal secretions, and to the keeping clean and free from these secretions the hands and other parts of the body as well as the clothing, vigilance should not thereby be relaxed in dealing with all the secretions in a sanitary manner.

Studies of the manner of travel of and the route taken by the disease in thinly populated districts especially have failed in not a few instances in supporting fully the idea of the human agency in the transmission of the infection. Studies of this kind cannot be made satisfactorily in cities or even in towns for the reason that the contact with persons is too frequent and promiscuous to permit of accurate tracing. Owing to this discrepancy, some other agencies have been invoked to account for the transmission of the infection over wide areas, and the chief ones of this character have been domestic animals and insects. Paralytic diseases among domestic animals are known and not highly infrequent. They have been noted among dogs, horses and fowl, but thus far it has not been found possible to correlate the paralytic diseases of the lower animals and those of man. Perhaps the most frequently observed coincidental paralytic diseases have been between hens and human beings. Undoubtedly since the wide prevalence of epidemic poliomyelitis, the existence of a paralytic disease among barnyard fowl has been more commonly noted. Possibly the condition has not actually become more frequent, but owing to the circumstance mentioned it has been oftener observed. It would appear that the paralysis among fowl is caused not by lesions of the central nervous system, but by lesions of the peripheral nerves and that it is due to a peripheral neuritis. It has not been found possible to transmit by direct inoculation the paralytic disease from chicken to chicken, or from chicken to monkey, or from paralytic monkey to chicken (Flexner and Lewis). However, it has been found possible to develop the paralysis in the laboratory by keeping the chickens in confinement for some time, and by supplying them an unusual and doubtless improper form of food (Flexner and Clark). It has proved as little possible to transfer the paralytic affection of dogs from one individual to another by direct inoculation or from dog to monkey or from paralyzed monkey to dog (Flexner and Lewis). These failures do not, of course, exclude the possibility that a reservoir for the virus may exist among domesticated animals that do not even respond to its presence by developing paralysis or other conditions which could be recognized as resembling poliomyelitis in man. The manner of the action of the virus of poliomyelitis in rabbits provides an illustration which shows how necessary it is to avoid general deductions in this field. At first it was strenuously denied that rabbits could be infected at all with the virus of poliomyelitis, and the examples of supposed successful inoculation reported were entirely disbelieved (Krause and Meinicke, Lentz and Huntemüller); but it must now be accepted that young rabbits occasionally, but by no means generally, are subject to inoculation with the virus of poliomyelitis, at least after it has passed through a long series of monkeys (Marks). Apparently a small percentage only of the inoculated rabbits develop any obvious symptoms, and these die, as a rule, during convulsive seizures which come on suddenly. A given virus has up to the present been sent through a series of six rabbits, after which it has failed to be further propagated. From the sixth series it has been reimplanted on the monkey, in which animal typical paralysis has been produced (Marks). It remains to add that the rabbits which succumb to the inoculation do not show any characteristic lesion of the central nervous system or other organs, as far as has been determined. The monkey, on the other hand, invariably shows the typical lesions of the central nervous system.

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[1] Since this was written Landsteiner, Levaditi and Pastia (Semaine Medicale, 1911, No. 25, p. 296) have established the presence of the virus of poliomyelitis in the tonsils and pharyngeal mucosa of a child who succumbed to infantile paralysis during the acute stage of the disease.

Insect contamination with the virus would serve, were it proved not only to be an experimental possibility but to occur in nature, to clear away any present apparent discrepancies in the epidemiology of the disease. In this connection it should be stated that not only does epidemic poliomyelitis spread over a wide territory, but its spread is not promiscuous, but along the routes of human travel. Therefore insects that seek human habitations and routes of travel, that possess the power to migrate over a considerable territory, that affect all classes of society, that abound during the period of greatest prevalence of the disease, and that do not wholly disappear at any season, should be the first to come under suspicion. Many, if not all, of these conditions are fulfilled by the common house fly.

Laboratory-bred flies have been subjected to contamination experiments with the virus of poliomyelitis, from which it appears that they are capable of harboring the virus on their bodies in a living and infectious state for at least forty-eight hours. Moreover, it has developed that the virus also survives within the viscera of the insects for some time. (Flexner and Clark.) It should now be readily possible to secure flies from rooms in which cases of acute poliomyelitis are, in order to ascertain whether in nature they also become contaminated with the virus of the disease.

When we turn to the question of the control of poliomyelitis by the cure of the disease we refer of course to the reduction in the mortality and in the crippling effects which it causes. In respect to this question we find ourselves provided with scant knowledge that at the moment is capable of being applied practically. Experimental studies have shown clearly that recovery from the disease is effected by means of immunity principles that appear and persist for a long time—perhaps for years—within the blood. It has indeed been found possible in animals to apply the blood serum taken from recovered human beings and monkeys in such a way as to prevent the development of paralysis in monkeys following the inoculation of the virus (Flexner and Lewis). More recently still the fact has been ascertained that several larger domestic animals, including the horse, sheep, goat and pig, can be made to develop the immunity principles in their blood by subjecting them to injections of the spinal cord and brain of monkeys containing the living virus (Flexner and Clark). But these sera do not hold out any great hope of beneficial application in the treatment of developed poliomyelitis in human beings, for the reason that they are relatively weak in the immunity principles. An effort is therefore being made to approach the therapeutic problem through another avenue, namely, the employment of drugs. At the outset it is patent that since the drugs must come to act in the region of the central nervous system, the choice is restricted to those that beside possessing antiseptic properties can yet be applied to that sensitive part. We possess almost no drugs that exhibit the property of "internal antisepsis" so called, or in other words, are capable of exerting their antiseptic action in the interior of the body, in the presence of the proteins of the blood and tissues. Just here account should be taken of the pathogenesis of epidemic meningitis, since it is on it that the selection of the drug and the manner of its administration may come to be based. The evidence at hand points to the meninges as being the location of the primary lesion of the disease. It would seem as though the virus of poliomyelitis became first implanted on the leptomeninges, in which it developed, causing a cellular exudation that affects especially the blood-vessels, the partial obstruction of which leads to the secondary production of the lesions of the nervous tissue itself. It is indeed not excluded that a direct action of the virus of poliomyelitis on the ganglion cells takes place, but this effect, if produced, appears to be less general and constant than the effects on the meninges. Hence the problem that presents itself is one that has to do with the control of the primary meningeal lesions, that in turn are caused by the virus present within the interstices of their tissues, as well as doubtless, at some stage of the process, within the cerebrospinal fluid itself. What is required then are antiseptic drugs having a special power to destroy this virus, and of very low toxicity, that can be made to exert their principal action on the meninges and in the subdural space. We possess in hexamethylenamin (urotropin) a drug which fulfils certain of these conditions. It is an internal antiseptic of some power, and is eliminated in some degree from the general circulation into the subdural space (Cushing and Crowe). On empirical grounds the drug has already been administered in cases of epidemic poliomyelitis, but whether with any definite effect is not known. Administered to monkeys prior to or coincident with inoculation and repeated daily afterward, hexamethylenamin is capable in some instances of preventing paralysis, and in others of lengthening materially the incubation period of the disease (Flexner and Clark). However, its powers in this direction are limited. On the other hand, its chemical composition is such as to permit of the addition of other chemical groups to the original molecule, in virtue of which the antiseptic power may be intensified. Through the employment of this means, a number of relatively non-toxic compounds have already been produced, which far exceed in internal antiseptic value the original drug. and some of these have already been applied experimentally with some degree of success to the prevention of the development of the paralysis following inoculation of the virus (Flexner, Jacobs and Clark). Whether any of these drugs will prove applicable to the treatment of human beings the victims of poliomyelitis it would be hazardous to predict, but it seems not improbable that some advance should be made along this line of investigation.

The case for the treatment of human beings is less hopeless, as I view it, than is commonly believed. It should be taken into account that much of the supposed damage inflicted on the nervous system of human beings at the onset of the paralysis is remediable. For the brunt of the disease falls not on the nervous tissue, but on the meninges, where it can in turn be opposed by therapeutic measures; and the severer nervous lesions are not in the most instances absolute, but they are merely relative and often probably merely functional in nature, since as many as 25 per cent. of the paralyzed may make complete recovery, and there is restored to a far larger percentage, by the usual processes of delayed resolution, a considerable degree of power in and use of muscles once severely paralyzed.

INFANTILE PARALYSIS

THE MOST PROMISING OUTLOOK FOR IMPROVEMENT IN TREATMENT FROM THE STANDPOINT OF THE PEDIATRICIAN

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GENERAL STATEMENTS

We now know that epidemic infantile paralysis is a result of an infective process produced by a specific virus which affects particularly the vessels of the meninges, leading to marked hyperemia, infiltration and inflammation, and to secondary involvement and degeneration of certain of the adjacent nerve-cells and fibers. The disease itself is a self-limited one, terminated by the production within the organism of antibodies to the specific virus. The duration of the acute symptoms may vary from several days to as many weeks, when they may end fatally or in complete recovery, or may be followed by the palsy of one or more muscles, dependent on the site and the extent of the nerve affection. The early paralysis is always of greater extent than the residual palsy, and is due apparently to pressure on nerve trunks by the edema and infiltration of the meninges. It is only after the disappearance of these acute phenomena that the extent of the lasting palsy due to nerve degeneration can be ascertained.

The *treatment* of the disease as presented to the pediatrician consists, in the first place, (a) in an attempt to lessen the severity of the attack, (b) in an effort to render the patient more comfortable during the course of symptoms, and (c) in the prevention of deformities, the result of disturbed muscular balance; and secondly, in averting the spread of the disease from the patient to others.

DIAGNOSIS

In regard to the effort to alter the course of the disease there are at present great difficulties. The diagnosis of the malady can rarely be made from the symptoms until the development of the paralysis. It usually begins with a febrile onset accompanied frequently with sore throat or digestive disturbances and more or less general hyperesthesia and sweating. These are rarely sufficient to distinguish it from other infectious ailments. However, in an epidemic the occurrence of these symptoms in a patient should lead certainly to the suspicion of poliomyelitis. The diagnosis can be considerably strengthened by an examination of the spinal fluid. Here there is an increase in the number of cellular elements, particularly in the lymphocytes and in the protein contents of the fluid. The value of this aid in diagnosis was strikingly illustrated in a case reported by Dr. Frissell,[1] in which the symptoms of infection were present but physical examination otherwise negative. The condition of the spinal fluid sent to Dr. Flexner was found to resemble that seen in monkeys inoculated with the virus of the poliomyelitis, just before the onset of paralysis. By the same means the presence of meningitis, often difficult to distinguish clinically from certain forms of infantile palsy, can usually be excluded.

The laboratory may also be of assistance in the diagnosis of the disease by testing the sera of the suspected patient on monkeys; if the condition is poliomyelitis the blood-serum of the patient mixed with an active virus *in vitro* will neutralize it and the effect of the mixture when injected into a susceptible animal will be *nil*.[2]. This method would be particularly serviceable in the recognition of sporadic and unusual cases in their early stages.

The disease, then, being recognized or suspected, have we any means at hand to control its course? Certainly none that is specific or satisfactory. Active immunization by intracranial injections of the virus has been repeatedly carried out with success in susceptible monkeys,[2] but a sufficiently active curative serum to be of therapeutic value for human beings has not yet been obtained, although serum from immunized animals or from those recovered from the disease will protect a susceptible monkey when injected intraspinally twenty-four hours after the injection of the virus. More hopeful as a therapeutic agent is the administration of hexamethylenamin (urotropin). Cushing, Crowe, Morris and others have shown that after the admininstration of this drug formaldehyd quickly appears in the blood and secretions of the body, including the spinal fluid, and it is thought that this antiseptic may destroy the virus, or at least deter its action in the congested meningeal vessels and on the nerve-cells.

On the ultimate result of treatment with this drug and with closely related products it is too early to speak positively from clinical experience. The number of cases in which good results are reported from the use of hexamethylenamin in small doses by the mouth is constantly growing and there is considerable experimental evidence in its favor.[3]

Thus it was found at the Rockefeller Institute, when the active virus was injected intracerebrally into monkeys, to which hexamethylenamin had been given for some time, in a proportion of these animals the incubation period of the disease was prolonged and in some the paralysis was entirely prevented. The effect of hexamethylenamin is probably not lasting and it gives no increased resistance to reinfection at a later period. It does, however, hold out some hope that if given before the paralysis begins this may be diminished, and it may be serviceable also in preventing the escape of the virus from the body.

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[1] Jour. Am. Med. Assn., 1911, lvi, 661.

[2] Jour. Am. Med. Assn., 1910, lv, 1105.

[3] Jour. Am. Med. Assn., 1910, lv, 1804.

TREATMENT

The duty of the physician to his patient is by no means completed in his rather unsatisfactory attempt to make a diagnosis and to lessen the severity of the malady. He can do much to make the child more comfortable. He is dealing with an infectious disease and one associated usually with more or less discomfort or pain. Complete *rest* is the first and most essential factor in the treatment of the disease. This must be secured, with an abundance of fresh air, preferably in the open.

The patient should be kept perfectly quiet and, better, completely isolated. The bowels should be opened and moved regularly and the diet should be light and nutritious as in other febrile conditions.

The suggestion of Lange[4] and Hohman[5] that the spinal column should be immobilized in a plaster cast will probably be serviceable in those cases in which the pain is particularly severe. Occasionally sedatives, best codein or morphin, may be necessary.

Cupping near the spinal column by the Bier method has many advocates, but it is doubtful whether intraspinal congestion can be relieved by this method.

A warm bath or pack with a cool application to the head may have a quieting effect in the early stages. The administration of nerve tonics, especially of strychnin, and of irritating procedures, such as electrical treatment or massage, must be carefully avoided at this time.

When the acute symptoms have subsided the patient enters the second stage of the illness, in which, although the fever has gone, there may be sensitiveness along the nerve trunks and on passive motion; there may be also contraction of the limbs due to pain which does not allow them to be brought into their normal positions. It is important that the absolute rest should be continued and that any over-stretching of paralyzed muscles, either from pressure of bed clothes or from gravity or from the pull of sound muscles should be prevented by the arrangement of sand bags, pillows, etc. At this time, heat as a moist or dry pack may relieve the tenderness.

The patient may be said to enter on the convalescent stage of the disease when the sensitiveness has disappeared and there are no contractions due to irritation. This stage lasts, as pointed out in the admirable report on infantile paralysis in Massachusetts in 1909, until all potential power has been regained and until the deformities require no further attention. It is important to emphasize the fact, not sufficiently understood by the physician, that the muscle power returns continuously, though slowly, through months and even years, and during all this period repeated observations and treatment are indicated.

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[4] Tr. Am. Pediat. Soc., 1910, xxii, 170.

[5] München. med. Wchnschr., 1909, lvi, 2508.

It should be the special endeavor at this time to prevent deformity and assist in the recovery of nerve and muscle power. The normal balance of the muscles about the joints should be maintained at all hazards, and the over-stretching of paralyzed muscles by the contraction of unaffected opposing muscles should be prevented. Judson[6] has emphasized the value of keeping the patient long in a recumbent position. He feels that the large predominance of the residual paralysis in the lower as compared to the upper extremity is due in part to the attempt of the patient to sustain his weight on the impaired muscles in the legs and feet. No corresponding exertion is demanded of the arms and hands. He suggests in many cases to extend the recumbent position so long as eighteen months.

The means at hand for stimulation of nerve and muscles are electricity, faradic when possible, and when response to this is lost, a galvanic current should be used; applications of various forms of heat, for the improvement of the circulation and the prevention of the comparatively low temperature of the paralyzed muscles, and massage, which improves the circulation and supplies artificial stimulus to both nerves and muscles. All these measures, however, are claimed by Sachs[7] and Strunsky[8] and others to be of much less value than what may be called *muscle training*. Strunsky in a recent article insists that the dominant element of success in the restoration of function is in *suggestion*, in securing the *cooperation* of the patient in the effort to make the desired movement, and that massage, passive motion and electricity, when helpful, are so because they are means of obtaining this end. "A bright child," he says, "one susceptible to impressions, makes better progress during the treatment than the stupid child." "Well directed massage may be the instrument that arouses the will power to concentrate to the utmost during muscular contraction, and leads to the building up of the mental and motor brain cells." An interesting contribution to this subject might be made on paralyzed monkeys and a comparison instituted between the prevention of atrophy or the restoration of function to muscles treated by electricity, by massage or by having such animals attempt voluntarily to make certain special movements. Microscopic examinations of such material might be instructive.

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[6] Denver Med. Times, Oct. 1, 1907.

[7] Jour. Am. Med. Assn., 1910, lv, 48.

[8] Am. Jour. Dis. Child., 1911, i, 266.

The surgical treatment of deformities resulting from infantile paralysis such as muscle and tendon transplantation and nerve grafting, or a discussion of the many effective mechanical devices for preventing and correcting deformities, does not fall within the scope of this paper. It remains only to refer briefly to the prevention of the spread of the disease from the patient to others.

Mention has already been made of the probable value of hexamethylenamin or similar germicidal drugs. It may be that the administration of this drug to those in attendance on a patient suffering from infantile paralysis may diminish their susceptibility to the disease. It should certainly be given to the patient during the acute stages, not merely for its possible effects on his infection, but because by this means the danger to those exposed may be lessened.

The studies at the Rockefeller Institute have shown that at least one portal of entry of the virus is in the nasopharynx and that the virulence of the virus is destroyed by the application of 1 per cent. hydrogen peroxid. It is rational, therefore, to apply this disinfectant to the nasopharynx of both patient and attendant at frequent intervals, and as Osgood and Lucas[9] have shown that the virus may persist for at least five months or longer in the nasopharynx of monkeys, this treatment of the patient should be continued, at perhaps longer intervals, for a more or less indefinite period.

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[9] Jour. Am. Med. Assn., 1911, lvi, 495.

THE RÔLE OF MINERAL SALTS IN THE METABOLISM OF INFANTS *

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It is the purpose of this paper to present, in rather broad outlines, the part which mineral salts play in carrying on the physiologic functions of the body, and in what manner they contribute to the various pathologic processes to which the infant and young child are subjected.

This field of metabolic research has been the last to be undertaken, and just now we are coming to realize its vast importance, not only in connection with their own functions, but in connection with the influence they have on the metabolism of fat, protein and carbohydrate. The chief reason for having failed to realize the importance of the mineral salts in metabolism is that it has long been thought that the salts contributed in no way to the nourishment of the child. It has been only recently that they have taken their rightful place as indirect energy producers.

HISTORICAL

The first investigator to concern himself with the value of mineral salts was von Liebig,[1] who, as early as 1840, studied the action of mineral salts both in animal and vegetable life, and many of his early deductions have become firmly fixed as laws in the field of mineral salts metabolism. C. Voit[2] is another investigator whose work on the action of sodium chlorid, as early as 1860, first gave to that salt its prominence above all others in the human economy. Vierordt was also an indefatigable worker, and as early as 1877, from meager data then present, had calculated absolute and relative heat and estimated child's metabolism. J. Forster,[3] in 1873, added his convincing experiments on the necessity of the mineral salts to the continuance of life, and these were further reinforced by the work of Lunin[4] in 1881. As time advanced, the roster of those who worked in the field of mineral metabolism contains the names of many

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*From the laboratories of the Presbyterian Hospital and Cornell University Medical College.

[1] Von Liebig, J.: Chemie in ihrer Anwendung auf Agrikultur und Physiologie, 1876, p. 332.

[2] Voit, C.: Ueber den Einfluss des Kochsalzes auf den Stoffwechsel, München, 1860.

[3] Forster, J.: Ztschr. f. Biol., 1873, ix.

[4] Lunin, N.: Ztschr. f. physiol. Chem., 1881, v.

notable investigators, as G. v. Bunge, Michel, Keller, Loeb, Muller, Schlossman, Blauberg, Rubner, Huebner, Freund, v. Noorden, and in these latter days the work is being carried on enthusiastically by L. Langstein, L. F. Meyer, E. Schloss, J. A. Schabad and others abroad, and by Howland, Schwartz, Talbot, Veeder, and others in this country.

A GENERAL VIEW

In undertaking a problem of this kind, it is well at the beginning to take a general view, first of the physiologic action of the mineral salts as a whole, and then to study what has been definitely determined as to the action and influence of each of the mineral constituents. Then by inquiring into the mineral constituents of the new-born and of older children, one will be in position to learn the mineral needs of the growing organism, and, knowing them, to ascertain how best to supply them, and to study the factors which enter into the proper utilization of the salts ingested in the food and to determine whether or not this utilization is sufficient to meet the demands of the growing infant.

First, then, a general view of the physiologic action of the mineral salts as a whole. Physiologists are generally agreed, and their findings confirmed by physiologic chemists, that the important functions of the mineral salts are as follows:

1. They maintain the osmotic pressure in tissue cells, blood, and body fluids; controlling the flow of water to and from tissues; any deviation from normal causing a shrinking or swelling of tissue cells.

2. They regulate the reaction of the blood and tissue fluids. A deviation from this reaction inhibits the action of the various ferments, delays chemical processes, and if such reaction suffers much variation, death results.

3. Their presence in tissues and fluids gives rise to irritability of muscle and excitability of nerve through the action of their respective *ions*. Through this function the rhythmical contractions of the heart are maintained.

4. They act as catalysts for a large series of chemical reactions which take place during the processes of absorption, retention, utilization, and form combinations with waste products of metabolism in order to effect their elimination; for example, they act as carriers of excess acid materials in oxidation processes.

5. They share in the upbuilding and growth of the body, since they are a constituent of every cell; particularly do they take part in the changes which go on in the albumin bodies as they become intimately bound with the body proteins.

6. Their function in the intermediary metabolism of the ductless glands is very apparent from the large quantities of mineral salts found in these glandular organs.

7. Through a most excellent self-regulation, they protect against the acid poisons which the body is constantly producing.

8. Through the work of the various *ions*, electrically charged, some positively, some negatively, many important functions are being assigned to them, such as controlling body-weight, temperature, regulating the pulse, increasing leukocytes, etc. These and many more functions, not clearly defined, depend on the presence of the mineral salts in the body, and not on their presence alone, but their presence in definite relationships to one another.

ABSOLUTE NECESSITY OF SALTS

While physiologists have been busy defining the various functions of salts, other investigators have determined the absolute necessity to the maintenance of life of a certain quantity of mineral salts, and not only a certain quantity, but they have found that these salts must be in certain organic combination, as the following experiments will show:

> Forster,[3] in 1873, fed pigeons on approximately ash-free diet, and found their bones brittle, and they all died within a month. He also fed dogs on salt-poor diet, and they lived from twenty-six to thirty-six days.
>
> Lunin[4] showed by his classic experiment that the salts must be in organic combination to be available. He found that mice thrived well on dried whole milk, but that if the salts were extracted from the milk, and they were fed only the protein, fat and carbohydrate, they shortly died, and further, after abstracting the salts, if he substituted the same quantity of other mineral salts, adding them to the protein, fat and carbohydrate, the mice died. Furthermore, mice fed on ash-free food, plus sufficient sodium carbonate to take the place of the usual salts, lived twice as long as mice fed only on ash-free diet; nevertheless, they succumbed, demonstrating that even with the necessary amount of bases carbonates cannot supply the salt needed.
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> Rohmann[5] added further confirmation to the value of salts. He fed mice a mixture of simple organic and inorganic food-stuffs. These mice lived and were able to produce young, but the latter could not be raised on artificial food, nor could they be made to produce living young.

It is evident from this latter experiment that artificial foods may be sufficient for the adult, whose supply of minerals is well established, but it is not sufficient to produce healthy offspring.

Abderhalden[6] believes that the same physiologic importance of salts exists for the animal kingdom as has been shown by von Liebig and others to exist for the vegetable kingdom.

The salts have a very important bearing on the absorption and retention of other food constituents, e. g., in a large nitrogen retention there is usually a large ash retention, and when ash is eliminated in large quantities there is usually an accompanying loss of nitrogen.

T. B. Robertson[7] points out how intimately the precipitation and coagulation of protein depends on the salts present in the solution as *ions*. Indeed it is becoming more and more to be appreciated that the various food constituents have a very intimate influence, the one on the other, and it is along this particular line that metabolism studies are directing themselves.

Recognizing, then, that the mineral salts are necessary to life, let us inquire what salts, and in what proportion in the body, Nature has stored

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5. Rohmann: Klin.-therap. Wchnschr., 1902, No. 40.
6. Abderhalden: Physiological Chemistry, p. 356.
7. Robertson, T. B.: Jour. Biol. Chem., May, 1911.

them, by the action of which not only life is maintained, but energy developed and growth permitted. We are indebted to a number of investigators for information on the ash-content of the human organism both during fetal life and later.

Fehling[8] gives us the following figures of the ash-content at different periods of fetal life:

Period of Life.	Ash Content; Per Cent. of Total Weight.
Fetus, 6 weeks	.001
Fetus, 4 months	.98
Fetus, 5th month, first half	1.4
Fetus, 5th month, second half	1.43
Fetus, 6th month	1.94
Fetus, 7th month	2.94
Fetus, 8th month	2.82
Fetus, 9th month	3.3
In the new-born	2.7
In the adult	4.4

It will be noted, therefore, that from the earliest observation of fetal life to those on adult bodies, there is a gradual increase of the ash-content. This increase is most rapid in terms of percentage of body weight during the fetal period, and thereafter the increase is much slower.

Let us now ask ourselves the question as to the mineral constituents contained in the total ash-content and study their relative amounts. Hugounencq[9] has given us this information for fetal life, and Soldner[10] for the new-born. Soldner found that there was 75 gm. of ash in a new-born child which was equal to 2.7 per cent. of its body weight, or 9.4 per cent. of the dry residue.

Total Ash in Parts Per 100

Period of Life.	Cl	P_2O_5	SO_3	CaO	MgO	K_2O	Na_2O	Fe_2O_3
Fetus, 5 months	8.59	34.36	1.8	32.5	1.58	8.28	12.62	.4
Fetus, 6 months	7.75	34.94	1.78	34.6	....	7.21	10.62	.39
Fetus, 7 months	8.53	35.39	1.46	34.13	1.17	8.45	10.95	.398
New-born (Soldner), average of 6	6.61	.....	2.02	38.08	1.43	7.06	7.67	.83

Soldner, arguing from the average ash content of six new-born infants, concluded that there was a daily need of 1.4 gm. of mineral ash, and an infant should retain of the intake, chlorin 14 per cent., potassium 11 per cent., sodium 35 per cent., CaO, MgO and P_2O_5 at least 65 per cent. of the intake.

It will be noted that phosphorus and calcium make up considerably over half; sodium about an eighth, and potassium and chlorin about a twelfth of the total ash-content, and that sulphur, magnesium and iron make up but a small part of the total.

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8. Fehling: Cited by Freund, in Pfaundler and Schlossman, i, 363.
9. Hugounencq: Compt. rend. Soc. de biol., li, 537.
10. Camerer and Soldner: Ztschr. f. Biol., 1900-3, xxxix, xl, xliii, and xliv.

Bunge,[11] after a careful study of the mineral contents of the milk of lower animals and estimating the daily requirements of their offspring, attempted to show that the ash-content of the body was in correct proportion to the ash-content of the various animals. But when this was applied to the nursing infant his analogy failed, and the problem did not solve itself as readily as this hypothesis would indicate. It is evident that the main metallic elements are calcium, sodium, potassium and magnesium; the main acid salts being phosphoric, hydrochloric, carbonic and sulphuric, calcium phosphate being the most abundant of all the salts.

It should be further noted that the phosphorus and calcium content of the body increases in percentage, and that the other elements remain at the same or less percentage, but of course their absolute amount gradually increases.

The difference between the ash-content of a new-born and the ash-content of a 4-months' old child represents the change which must take place in the mineral salt storing. In actual figures the child must add to his weight, during the first four months, the following quantities of the various minerals:

	Gm.
K_2O	2.0
Na_2O	2.57
CaO	11.75
MgO	.31
Fe_2O_3	....
P_2O_5	10.48
Cl	1.12
S	....

It will be noted what really small quantities of the mineral salts are added to the body—extremely small when we consider the large quantity which a child during the first year must ingest. It is estimated that only about 4 per cent. of intake goes to growth in early months and later only half that amount. It is evident that a large quantity must be worked over. Taking mother's milk as a basis, during the first twelve months of life there is approximately 800 gm. of total ash ingested. This is divided among the various mineral salts as follows:

	Gm.
K_2O	276.
Na_2O	19.6
CaO	157.6
MgO	27.2
Fe_2O_3	8.0
P_2O_5	117.6
Cl	117.6
SO_3	57.4
Total	791.0

If we take cow's milk as a basis, the picture is entirely different. Taking the average amount fed as outlined in Dr. Holt's text-book, an infant would ingest approximately 1,500 gm. of total ash during the first year of life, which would be divided among the various mineral constituents as follows:

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[11] Bunge: Cited by Freund, Pfaundler and Schlossman, Vol. i.

	Gm.
K_2O	377.0
Na_2O	93.0
CaO	344.0
MgO	41.0
Fe_2O_3	4.2
P_2O_5	487.4
Cl	84.0
S	69.4
Total	1,500.0

This naturally leads us to a two-fold conception of the use which the body makes of the salts. First, a certain small per cent. is firmly bound with the tissues of the body and only escapes when such tissues are destroyed in oxidation; and a second group which are simply held in solution in the body fluids ready to be excreted, or to act as bases or alkalies to take up the products of cell destruction, or combine with acids set free in the processes of catabolism, or in the form of *ions* to subserve definite physiologic functions. It should be borne in mind that only a small part of the mineral salt intake in any day's feeding is added as an integral part of the tissue. and that by far the largest part is simply held in solution awaiting its excretion, either through the skin, urine or back into the intestinal canal. With sulphur and phosphorus the problem is a little more complicated, as these two substances are in exceedingly close chemical relationship with albumin, and before they can be set free the foreign albumin molecule must be torn down before it can be again rebuilded into the tissue substance and fluids of the host.

Having noted just what minerals and acids are present in the body at the end of fetal life, it behooves us to inquire into the method by which we can continue to supply the needs of the infant as relates to its mineral constituents so as best to foster its normal growth and aid in supplying its daily energy requirement. Nature has supplied us with a most excellent criterion by which we may reach a solution of this problem, viz., in normal mother's milk. Let us, therefore, address ourselves to a study of Nature's method of supplying the need of the growing infant by carefully considering the mineral constituents and their relative proportions in mother's milk.

In early mother's milk, i. e., colostrum, according to Camerer,[12] we have a marked increase from the first to the seventh day in the ash-content as follows:

Day after delivery	1	2	3	4	5	6	7
Ash content in per cents	0.1	0.5	0.7	0.9	1.0	1.1	1.3

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[12] Camerer: Cited by Freund in Pfaundler and Schlossman. i, 386.

Thus Nature provides in the early nursing period for a very rapid increase in the mineral constituents of the food. In mother's milk there is about 2.0 gm. of total ash to 1,000 gm. of milk. This 2 gm. of ash is divided among the various mineral constituents according to various authors, as follows:

In 1,000 gm. of mother's milk, there is, according to

	Bunge 1[15] Gm.	Bunge 2[15] Gm.	Camerer[13] and Soldner	Blauberg[14] Gm.
K_2O	0.780	0.703	0.884	0.69
Na_2O	0.232	0.257	0.357	0.049
CaO	0.328	0.343	0.378	0.394
MgO	0.064	0.065	0.053	0.068
Fe_2O_3	0.004	0.006	0.002	0.02
P_2O_5	0.473	0.469	0.310	0.294
Cl	0.438	0.445	0.591	0.294
SO_3	....	.....	.....	0.143

The ash-content of mother's milk does not remain constant, as is shown by Soldner[16] in his examinations of mother's milk on the eighth and seventieth days. In 1,000 gm. of mother's milk on the eighth day, there was 3 gm. of total ash, and in the same quantity on the seventieth day there was 2 gm. of total ash divided as follows:

	Eighth day Gm.	Seventieth day Gm.
K_2O	1.008	.259
Na_2O	.448	.176
CaO	.376	.381
MgO	.054	.052
Fe_2O_3	.0022	.00125
P_2O_5	.320	.288
SO_3	.096	.063
Cl	.716	.342

From the above, it would seem that the fixed alkalies K and Na diminish greatly as does also the chlorin content of the milk, while the bone-forming constituents, viz., calcium, phosphorus and magnesium, remain nearly constant. In cow's milk the relations are entirely different as is shown by the exceedingly large ash-content of 7.8 gm. per 1,000 gm. of milk as against 2 gm. in 1,000 gm. of mother's milk. Not only does cow's milk contain more ash, but in vastly different proportion of mineral constituents than mother's milk, as will be seen by the following table when compared with the preceding table showing mineral contents of the ash of mother's milk. In 1,000 gm. of cow's milk there is:

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13. Camerer and Soldner: Cited by Albu-Neuberg, Mineralstoffwechsel, p. 51.

14. Blauberg: Cited by Langstein and Meyer Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, page 15.

15. Bunge: Cited by Albu-Neuberg, Mineralstoffwechsel, p. 51.

16. Soldner: Cited by Freund, in Pfaundler and Schlossman, p. 377.

	Bunge[15] Gm.	Soldner[13] Gm.	Hoobler Gm.	Soldner[17] Gm.
K_2O	1.766	1.720	.....	1.885
Na_2O	1.110	0.51	.....	0.465
CaO	1.599	1.980	1.600	1.72
MgO	0.210	0.20	0.167	0.205
Fe_2O_3	0.004	.....	.....	0.021
P_2O_5	1.974	1.82	2.140	2.437
Cl	1.697	0.98	1.86 (NaCl)	0.820
S	....	.....	0.33638	....

It will be seen that in the same quantities of milk, that of the cow contains over twice as much potassium, five times as much sodium, phosphorus and calcium, four times as much magnesium and chlorin and six times as much sulphur. And, further, these salts are not in the same organic combination in one as in the other, as shown by Keller,[18] and also by Schlossman,[19] as relates to phosphorus, and when we consider that it is the organically bound salts only, as shown by Lunin,[4] which are available, this factor is a very important one.

Not only are the salts organically bound, but there is a peculiar specificity about the whey containing the salts of mother's milk. Meyer[20] has shown that not only the protein and fat of mother's milk, but even the casein and fat of cow's milk, are well absorbed and retained when mixed with the whey of mother's milk. Children fed on the fat and protein of mother's milk mixed with the whey of cow's milk are not able to utilize these food products and do badly. It would seem that some constituent in mother's milk whey contains the essential dynamic force for making the casein and fat of both mother's and cow's milk available for nutritive purposes.

Having now considered separately the salts of the child's body and the salts of the two most common foods, let us study the processes which take place when these foods are ingested by the infant. It would contribute to a continuity of thought if we were to follow each individual salt through its various metabolic steps under perfectly normal conditions and discuss them under the heads of ingestion, absorption, retention and elimination, considering the results obtained by investigators in the use of mother's milk and cow's milk.

After having considered these steps in normal metabolism, I shall address myself briefly to abnormal conditions of metabolism, desiring rather to give most attention to the consideration of the normal. I shall take occasion to consider, along with the findings of literature, some results obtained by me in a series of metabolism studies which I have

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[17] Soldner: Cited by Langstein and Meyer, Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, page 15.

[18] Keller, A.: Arch. f. Kinderh., 1900, xxix.

[19] Schlossman: Arch. f. Kinderh., 1905, xl.

[20] Meyer, L. F.: Cited by Meara, Problems of Nutrition in Early Life, Arch. Pediat., xxvii, 401.

TOTAL ASH

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent. of Intake	Per Kilo
Mother's milk (Blauberg)	1.13	0.193	0.373	0.937	82.9	....	0.56	49.5	....
Mother's milk (Blauberg)	1.32	0.24	0.47	1.08	81.8	....	0.61	45.9	....
Cow's milk (Soldner)	6.841	2.686	3.1341	4.15	60.7	....	1.013	14.8	....
Diluted cow's milk, 2.1% fat (Hoobler)	8.9691	4.2651	4.7966	4.7039	53.0	.565	......	....	....
Cow's milk, 4% fat (Hoobler)	9.4808	3.1390	3.0834	6.3418	66.8	.808	2.8917	43.5	.368
Cow's milk and cream, 5.4% fat (Hoobler)	8.7634	1.8675	4.1493	6.8959	78.6	.861	2.7465	37.8	.344
Cow's milk (Blauberg)	6.84	2.68	3.13	4.15	60.7	....	1.01	14.8	....

Figures given above are in grams in 24 hours.

carried out in the wards and laboratory of the Presbyterian Hospital on a perfectly healthy infant of 9 months who had been fed on cow's milk from the time of his birth, details of the experiment, as relates to nitrogen metabolism, having already been published.[22]

TOTAL ASH

I will first consider the figures covering the entire mineral metabolism as represented by total ash, and will then discuss its various phases.

INGESTION

First let us consider the intake. It should be remembered that mother's milk is relatively poor in ash-content while that of cow's milk is exceedingly rich, so that one is not surprised to note that the intake of total ash through breast feeding is very much less than with cow's milk feeding. From the figures of Blauberg, Soldner, and my own determinations, the ash intake in artificially fed children is from six to nine times greater than that of breast-fed children.

ABSORPTION OF TOTAL ASH

Various observers have recorded their findings of ash absorption in mother's milk, varying from 81.82 per cent. by Blauberg to 53 per cent. of intake by Schlossman; Biedert's determination was 77 per cent., and that of Rubner and Heubner 79.42 per cent., while the absorption of total ash of cow's milk by different authors is as follows (see also p. 115):

	Per cent.		Per cent.
Soldner	60.7	Biedert	65.1
Schlossman	70.	Hoobler	53.
Tangl	62.1	Hoobler	66.8
Blauberg	53.72	Hoobler	78.6

It will be seen that the absorption per cent. is 15 per cent. to 25 per cent. better on mother's milk, but because of the large intake the actual amount absorbed is very much larger in cow's milk feedings than in breast-fed. For example, 1.08 gm. was absorbed in twenty-four hours on mother's milk, while on cow's milk from 4 to 6 gm. were absorbed daily. Thus approximately four to six times more is absorbed in artificial feeding.

As we shall see later, this better absorption of mother's milk ash lies in the fact that calcium, magnesium and phosphorus are much better absorbed. As was demonstrated in my work on the various fat feedings, and now being published in the Presbyterian Hospital Report of this year, nitrogen, chlorin, sulphur and magnesium were absorbed in the same ratio as these elements existed in the food. The greatest variations from the ratio in the food occurred in calcium and phosphorus.

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[22] Hoobler: Arch. Pediat., 1910, xxvii, 853.

RETENTION

Without doubt the best criterion of availability and utilization of any given food-stuff is not its large per cent. of absorption, or even its large absolute amount of absorption; but rather the absolute amount retained. Literature does not yet contain reports which cover sufficient periods of investigation to feel quite sure that these so-called absolute retentions are permanent or simply transitory, since it takes weeks to utilize and eliminate the mineral salts. Therefore a prescribed diet should be carried out for weeks instead of days for most accurate results. However, the reports in literature show that the ash of mother's milk is well retained and this is but natural, for the salts come to the infant in much better form for utilization than in cow's milk.

In Blauberg's case on mother's milk (see total ash tabulation), the absolute retention was 0.61 gm., being 45.9 per cent. of the intake. In cow's milk feeding, the per cent. of retention is lower but the absolute amount is higher, owing to the much richer ash-content of the cow's milk. Blauberg's case on cow's milk feeding, having a retention of 14.8 per cent. of intake, represented an absolute amount of 1.013, being nearly twice the amount retained under mother's milk feeding. In my 9-month child there was retained 2.89 gm. or 43.5 per cent. intake. Blauberg found that with mother's milk feeding all the minerals were retained with the exception of sodium; in cow's milk there was a loss in Cl, S, and Na. It would seem that each child is a law unto itself so far as retention of mineral ash is concerned. It apparently takes it on just in accordance with the demands of physiologic growth.

In my determinations in connection with various strengths of fat in foods, I found that as compared with nitrogen retention, the retention of the mineral salts was relatively poorer. This poor retention was most marked on the lower fat food, better on the medium fat diet, and best as regards the absolute amount retained on the high (5.4 per cent.) fat diet. Retention of the salts in proportion to nitrogen was never in the same proportion as existed between the salts and nitrogen of the food.

ELIMINATION

The elimination through the feces and urine differs in amounts on mother's and cow's milk. In mother's milk feeding, one-third of the salts are eliminated through the feces and two-thirds through the urine, while in cow's milk feeding about half is eliminated by the urine and half by the feces, though the figures of different investigators vary. In my own figures the ash of the feces was three times as large on a 2.1 per cent. fat mixture as on a 5.4 per cent. mixture.

THE ANOMALIES IN THE METABOLISM OF TOTAL ASH

In the elaboration of Finkelstein's theory of food disturbances in infants and children, L. F. Meyer[23] has attributed to the mineral salts certain deleterious influences.

In each of Finkelstein's four stages of nutritional disturbance, Meyer finds that there is some anomaly in the salt metabolism. In the stage of *"Bilanzstörung,"* there is decreased retention of the alkaline earths. There is also a lessened retention of other salts.

In the stage of dyspepsia, the salt elimination by the feces is increased but the ash balance is not markedly changed. In the stage of decomposition the entire picture is determined by the loss of the mineral salts, particularly through the loss of the fixed alkalies. Through the fatty acids in the stools, the Ca and Mg are used up. The diarrheal stools of this period are due largely to alkali loss. The condition of relative acidosis of Steinits (and of alkalipenia of Pfaundler) takes place during this stage, due to the loss of alkali.

In the fourth stage, of intoxication, the salt metabolism is little known. There is a negative balance of chlorin and probably of the other mineral constituents. Whether the salt loss controls the water loss or vice versa is still a question, but since the urine is much decreased and the output of water by the feces is increased, it would seem that the salts were accountable for this diversion of the water elimination. It is evident that salts play an important part in every digestive disturbance of the infant and young child.

CALCIUM

The calcium need of the growing infant is well met through the abundance of its salts in the milk, either of mother's or of cow's. Calcium makes up one-fifth of the ash of mother's as well as of the ash of cow's milk. Calcium is taken into the body in organic and inorganic form. The organic combination is present in milk, yolk of eggs and vegetables, and the inorganic form in water used as a diluent and for drinking.

The importance of the calcium salts in the developing organism can hardly be overestimated. Physiologists[24] have shown that the calcium *ions* in the blood, though in small quantity, are yet absolutely necessary to the irritability of muscle. If calcium is present in too large quantities, as compared with Na and K *ions,* there is produced a tonic contraction known as calcium rigor.

Calcium has a definite specific action of its own and cannot be replaced by other earthy bases, as magnesium and strontium, as stated by Stewart.[25] The fact is well known that calcium is necessary to ferment action as shown by the coagulation of blood and the precipitation of casein in milk. Calcium is much the largest mineral constituent of the body. Its most common salt is calcium phosphate, which makes up a large part of the bone salts.

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[23] Langstein and Meyer: Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, pp. 111-166.

[24] Howell: Physiology, Ed. 2, 1907.

[25] Stewart: Physiology, Ed. 1910, p. 542.

Jacques Loeb[26] has shown the necessity of calcium salts for the development of the lower forms of life, and Blauberg has shown that children who cannot metabolize calcium cannot survive.

Mother's milk contains only about 20 per cent. as much calcium as cow's milk; therefore we would expect a considerable variation in its absorption and retention, as is shown by the following:

CALCIUM AS CaO

The calcium of mother's milk is 0.394 grams in 1,000 gm. I found calcium of cow's milk to be 1.6 grams in 1,000 gm., or nearly four times as much in cow's as in mother's milk. (See also tabulation page 120.)

It will be noted first that the calcium intake in cow's milk feeding is about eight times greater than in mother's milk; that the amount actually absorbed and retained is four times greater on cow's milk than on mother's milk. However, a much larger percentage of mother's milk calcium is retained. It is evident, therefore, that the calcium of mother's milk is much better metabolized than the calcium of cow's milk, and since a healthy nursing infant shows no signs of a deficiency of calcium, we may well consider the amount which it gets as being the true calcium need. The absorption of calcium depends in part on the presence of accompanying salts; for example, if much alkali bases are present in the intake the absorption is diminished, whereas NaCl assists in calcium absorption. Calcium is more readily absorbed on flesh than on a vegetable diet.

ELIMINATION

It should be noted that the elimination of calcium is almost entirely through the feces; only 5 to 10 per cent. of the intake appears in the urine. This does not mean that the calcium is not well absorbed, but that it is excreted into the large intestine, as is proved by the fact that larger quantities of calcium are found in the large intestine than in the small intestine. It was Voit[27] who showed that 0.15 gm. of calcium per day was excreted from the inner surface of the intestine.

The amount of calcium excreted in the urine of infants fed on breast and cow's milk does not vary greatly, but the amount which appears in the feces varies greatly, being in some instances twenty times greater. Calcium makes up a quarter or a third part of the dried feces of cow's-milk-fed children, as against a much smaller portion in breast-fed. The

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26. Loeb, J.: Cited by Meyer, Jahrb. f. Kinderh., lxxi, 1.
27. Voit: Cited by Howell, Physiology, Ed. 2, p. 834.

Calcium as CaO

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk (Blauberg)	0.2884	0.0952	0.0127	......	....	....	0.176	62.4	....
Mother's milk (Blauberg 5 mos.)	0.2720	0.0660	0.0310	0.2060	75.8	....	0.175	64.5	.026
Cow's milk (R. & H. 7½)	2.0824	1.142	0.0166	0.9370	45.1	....	0.924	44.4	.122
Diluted cow's, 2.1% fat (Hoobler)	2.0536	2.2687	0.0301	Negative	....	....	Negative	....	....
Cow's whole milk, 4% fat	2.0500	1.6962	0.305	0.3538	17.2	.045	0.3233	15.7	.041
Cow's milk and cream, 5.4% fat	2.0923	0.9515	0.0085	1.1408	54.5	.142	1.1322	54.1	.142

Figures given above are in grams in 24 hours.

form in which the calcium usually appears in the feces is that of the insoluble soaps, or in the form of calcium phosphate.

In my series of studies the elimination of calcium in the feces was greater on milk of lower fat content. As fat was increased in the food, the calcium was diminished in the feces. The calcium eliminated in the urine appears along with magnesium, bound with phosphoric, carbonic and uric acids. Iron is another mineral constituent which is excreted very poorly through the urine, and this leads one to group these two constituents together and to inquire if there are other characteristics. It should be noted that their presence in many organs, for example the thyroid gland, the liver, the spleen and the ovaries, suggests physiologic and chemical affinities as pointed out by Albu and Neuberg.[28] The internal secretions which play such a part in intermediary metabolism of the mineral salts, may be largely affected by the relationship of these two minerals. Calcium and phosphorus are closely allied in the bones, in the ovaries, and in the thyroid gland.

THE ANOMALIES OF CALCIUM METABOLISM

As a rule there is a great individual difference in the amount of calcium absorbed, and a further difference in the ability to retain the calcium absorbed. Rarely is such a condition due to the lack of calcium in the food, although many artificial foods are very poor in calcium. A diet containing less than 1 to 1.5 gm. CaO daily should be considered calcium-poor, except when on mother's milk feeding.

It has been shown that when calcium is purposely withheld from the diet of young puppies, rachitis develops, and the bones of young pigeons fed on calcium-poor diet are very fragile (Forster[3]). In the bones, in rachitis the mineral constituents are depleted, particularly calcium and phosphorus. The total ash of bones which normally is 65 per cent. falls to as low as 25 per cent. and the main loss falls on the calcium phosphate. The calcium loss in rachitis is largely through the intestine, with but little change in urinary calcium. In feces of rachitis, there is an increased elimination over that of healthy children, as shown by J. A. Schabad.[29] In rachitis particularly the weak point in the metabolism cycle may be the inability of the bones themselves to take up and build into bony tissue the calcium and phosphorus brought to them by the fluids, as has been pointed out by Albu and Neuberg.[28] The fact that calcium has much to do with the function of the nervous system has been shown by the calcium disturbances in tetany, as demonstrated by Schabad.[30] Further, the large proportional content of the brain tissue of the new-born in calcium

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[28] Albu-Neuberg: Mineralstoffwechsel, Berlin, 1906, p. 70.

[29] Schabad, J. A.: Arch. f. Kinderh., liii, 241.

[30] Schabad, J. A.: Monatschr. f. Kinderh., ix, No. 1; Jahrb. f. Kinderh., l, No. 1.

(0.168 per cent. CaO), as compared with an 8-year-old child's brain (0.05 per cent.) speaks further confirmation of this. There is a very appreciable loss of calcium from the nerve structures during the first year of life. Quest[31] found less calcium in the brains of children who died of tetany than of children of the same age without tetany.

Schloss[32] has more recently shown that subnormal body temperature in some cases depends on the presence of calcium *ions*. In the symptom-complex which Finkelstein calls *Ernährungstörung*, during the stage of *Bilanzstörung,* Meyer[23] has shown that there is a decreased retention of calcium due in part to the fact that the fats of the stools are increased, and these demand the alkaline earth to neutralize the fatty acids. There may be such a demand that not only will no calcium and magnesium be retained, but there may be an actual withdrawal of these salts from the body. This may account for a portion of the loss of weight in this stage of food disturbance.

IRON

Cow's milk and mother's milk contain about the same amounts of iron. Each is very poor in iron, and were it not for the relatively large amount stored in the liver and blood of the new-born there would be a deficiency in the early months of feeding. The following table shows that the form in which the iron is present has a large bearing on its availability. The iron of goat's milk is poorly absorbed and poorly retained, while the iron of mother's milk is well absorbed and well retained. Iron is eliminated almost entirely through the feces but a very small quantity through the urine.

Iron plays an important part in metabolism. It is specially important in the formation of the hemoglobin molecule. It acts as a catalyst in oxidation processes, especially in the group of nucleoproteins, as has been shown by Spitzer[44] and by Manchot.[45] Iron is presented for consumption in both the organic and inorganic form. The organic forms occur in the nucleoalbumins, in milk, yolk of eggs and in many vegetables.

IRON AS Fe_2O_3

In 1,000 gm. mother's milk, .02 gm. to .04 gm.
In 1,000 gm. cow's milk, .021 gm. (Abderhalden).

		Elimination		Absorption		Retention	
Food	Intake	Feces	Urine	Gm.	%	Gm.	%
Mother's milk	.00705	.00084	.00055	.00621	88.09	.00566	82.28
Goats' milk	.00344	.00259	.00009	.00085	24.71	.00076	22.09

Figures given above are in grams in 24 hours.

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[31] Quest: Cited by Freund, in Pfaundler and Schlossman, i, p. 285.

[32] Schloss: Cited by Langstein and Meyer, Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, p. 21.

[44] Spitzer: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 151.

[45] Manchot: Cited by Albu and Neuberg, Mineralstoffwechsel, p. 151.

MAGNESIUM AS MgO

In 1,000 gm. mothers' milk there is 0.068 gm. MgO.
In 1,000 gm. cows' milk there is .205 gm. MgO.

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk (Blauberg)	0.047	0.0157	0.014	......	....	....	0.0175	37.2	....
Cow's milk (Soldner)	0.15017	0.0944	0.03718	. ....	....	....	0.017	11.5	....
Diluted cow's milk, 2.1% fat (Hoobler)	0.10843	0.0058	0.0134	.10258	94.6	.123	0.0891	82.1	.011
Whole cow's milk, 4% fat (Hoobler)	0.07755	0.0300	0.04861	.04746	61.3	.045	Negative	....	....
Cow's milk and cream, 5.4% fat (Hoobler)	0.14999	0.0828	0.01909	.06719	44.7	.008	0.04809	32.0	.006

Figures given above are in grams in 24 hours.

MAGNESIUM

Magnesium and calcium are very closely connected in the metabolic function. They occur in the organism in much the same places and as salts of the same acids. Their proportion is CaO:MgO::40:1. Magnesium has a little wider distribution in the body tissues than does calcium. The latter occurs almost entirely—at least 99 per cent.—in the bones, while magnesium is found in muscle-tissue as high as 0.04 per cent. The part which magnesium plays in bone structure is important. Magnesium makes up about 10 to 15 per cent. of the total ash of bone. The relation of magnesium in these structures is about 1:9. The magnesium table on page 123 indicates that the Mg need of the growing infant on mother's milk is 0.047. Bunge, as cited by Albu and Neuberg, gives the magnesium need as 0.6. This seems rather high, for, since there is about 0.06 gm. Mg in a litre of mother's milk, it would require 10 litres to satisfy this need. Blauberg's breast-fed infant got but 0.047 gm. daily. The intake when fed on cow's milk varied; according to Soldner the daily intake was 0.15 gm., while my determinations showed intake varying from 0.07 to 0.15.

ABSORPTION

The absorption of magnesium which takes place through the small intestine is relatively very good. My determinations gave 94.6 as the per cent. of intake which was absorbed when feedings were low in fat. As the fat content of the food was increased, there was relatively poorer absorption, the percentages being 61.3 on a 4 per cent., and 44.7 on 5.4 per cent. fat mixture.

RETENTION

The retention of magnesium in my series was better on 2.1 per cent. fat mixture than on the 5.4 per cent. mixture. This retention varied inversely with the calcium retention so far as the amount of the fat in the food is concerned. In my findings for calcium, retention was poorest on lower fat mixtures and improved on the higher fat mixtures.

ELIMINATION

Excretion occurs both through urine and feces. On mother's milk in Blauberg's case, the excretion through either channel was about the same, while in cow's milk in some instances it was higher in urine and in others it was higher in the feces. In any event, the excretion is very small and that through the urine occurs as triple phosphates.

ANOMALIES OF RETENTION

There is more or less relation between Ca and Mg in the formation of oxalic acid concretions. It has been found that if the ratio of CaO to MgO be as 1 to 0.8 the concretion may be kept in solution. The smaller

Phosphorus as P_2O_5

	Total Gm.	Organically Bound, Gm.
In 1,000 gm. mother's milk	.294	42.3
In 1,000 gm. cow's milk	2.437	46.
In 1,000 gm. cow's milk (Hoobler)	2.140	....

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	0.2768	0.0363	0.0481	......	....	....	.192	69.13	.....
Mother's milk, 5 mos.	0.2030	0.0220	0.088	0.1810	89.1	....	.093	45.9	.0138
Cow's milk	1.4429	0.5352	0.5003	......	....	....	.4074	30.7	.....
Cow's milk (Keller's 2¾ mo)	0.8248	0.1073	0.4106	0.7174	87.1	....	.3068	37.2	.0626
Cow's milk (Blauberg's 7½ mos.)	2.0605	0.9627	0.5899	1.098	53.28	....	.5079	24.2	.0671
Diluted cow's milk, 2.1% fat (Hoobler)	2.2155	0.7648	1.152	1.4507	67.0	.174	.3320	14.5	.040
Cow's milk, whole, 4% fat (Hoobler)	2.7418	0.59914	2.009	2.1426	78.1	.274	.1336	4.8	.0171
Cow's milk and cream, 5.4% fat (Hoobler)	2.2346	0.3789	1.336	1.8556	83.0	.235	.6196	27.7	.0657

Figures given above are in grams in 24 hours.

the calcium and the larger the Mg content the easier becomes the solution of calcium oxalate.

PHOSPHORUS

Of all the mineral elements, perhaps none has been studied more assiduously than phosphorus. Phosphorus is brought into the body in two very different forms, viz., that which is organically bound, occurring in milk, eggs and legumes, and a small part as phosphoric acid. When in organic combination it is found as nucleoalbumin, nuclein, vitellin, casein and lecithin.

The source in which we are most interested is that of mother's and cow's milk, and these two foods differ considerably in the amount of organically bound phosphorus. Mother's milk contains 0.31 to 0.45 gm. per liter of P_2O_5, while cow's milk contains 1.81 gm. P_2O_5 per liter. Keller[33] has shown that of the phosphorus of mother's milk 77 per cent. is organically bound, while in cow's milk only 27.9 per cent. is so bound. Of this organically bound phosphorus 54 per cent. occurs as nucleophosphorus in mother's milk, and but 13.4 per cent. in cow's milk, so that it is very evident that the phosphorus of cow's milk, though larger in actual quantity, is not in such form as to be available, as is the case of mother's milk. The nucleins of milk make up 41.5 per cent. of the total phosphorus of mother's milk, while of cow's milk only 6 per cent. is in that form. In mother's milk 35 per cent. of total phosphorus is in the form of lecithin, while the lecithin of cow's milk is but 5 per cent. according to Stocklasa.[34]

The form in which the phosphorus reaches the organism is important for Salkowski has shown that the organism has not the power to build from phosphorus-free albumin, or from inorganic phosphates, cells which require as an integral part organically bound phosphorus.

Indeed, it has been shown that the phosphorus absorption is not in the least affected by the presence or absence of inorganic phosphates, but, on the other hand, the phosphorus absorption may be greatly increased when a child is fed on yolk of egg as shown by Cronheim and Muller.[35]

Phosphorus is in demand in the body, particularly in glandular structures and bones, and for the central nervous system, and we should expect to find a considerable daily need on the part of the growing organism. This need seems satisfied in the healthy breast-fed infant on an intake varying from 0.7 to 0.8 gm. as a minimum and 1 to 2 gm. as a maximum. This is a wide variation, but we should consider that phosphorus is one of the minerals which becomes a definite part of the tissue structures throughout the body, and by virtue of its close connection with the albumin molecule must likewise suffer destruction along with the albumin, therefore it varies with the protein need.

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[33] Kellar, A.: Arch. f. Kinderh., xxix, Stuttgart, 1900, p. 1.

[34] Stocklasa: Ebenda, 1897, xxiii.

[35] Cronheim and Muller: Ztschr. f. diät. u. physik. Therap., 1903, vi.

The investigators who have determined phosphorus balances on infants are Blauberg, Michel, Keller, Cronheim and Muller and Schlossman. Let us consider some of their findings in comparison with the determinations which I have made.

ABSORPTION

It will first be noted that the intake of phosphorus is nearly ten times as great for cow's milk as for mother's milk and that in both forms of milk feeding the per cent. of intake absorbed indicates a very good absorption ability. In mother's milk, the absorption per cent. is 89.2 and that of cow's milk 53.2 in Blauberg's case. My determinations were 67.0 per cent., 78.1 per cent. and 83.0 per cent. on low, medium and high fat feeding. From this it would seem that phosphorus is more readily absorbed in the presence of increasing quantities of fat. The amount of the absorption depends more on the kind of phosphorus than on the quantity. The absorption of phosphorus is hindered when there is a relatively high ratio of accompanying alkaline earths and alkalies in the food; for example, when vegetables are fed a large calcium intake is present. This forms insoluble salts of phosphorus in the intestine and thus absorption is prevented. However, when these two elements meet within the body, they are joined in exceedingly close metabolic activity.

From my own determinations it appears that the phosphorus and nitrogen absorption varied considerably from the ratio in which these elements occurred in the food. Phosphorus absorption was relatively less than nitrogen absorption, during the low (2.1 per cent.) fat feeding, and was best in the medium fat feeding (4 per cent.), where it approximated the ratio which existed between nitrogen and phosphorus in the food.

RETENTION

The retention of phosphorus is one of great importance to the existence of life, for in conditions of starvation the organism clings tenaciously to its phosphorus—perhaps more so than to any other mineral constituent, except NaCl. This is probably due to its close connection with the central nervous system, for at the end of long periods of starvation the phosphorus content of nervous tissue is very little impoverished. This retention is, no doubt, in proportion to the need, and not only the present need, but it is stored up for an emergency; for the animal organism when fed on phosphorus-rich diet not only brings itself into phosphorus equilibrium, but retains a part of this excess phosphorus. The retention keeps step with the need and gradually diminishes when the skeleton is well formed.

As in the case of absorption, the phosphorus is retained not so much in proportion to its amount as according to the kind present. Its retention runs parallel with that of nitrogen in cases studied by Keller,[33] but L. F. Meyer[36] has been unable to confirm this finding, and in my determinations phosphorus and nitrogen were not retained in proportional amounts, i. e., 29.5 per cent. food-nitrogen was retained while only 4.8 per cent. of food-phosphorus was retained.

ELIMINATION

The elimination of phosphorus takes place both through the feces and through the urine. In most instances it is about equally divided between these two channels of excretion. However, great variations occur, for example, in children on a vegetable diet which contains much calcium, the phosphorus is largely excreted through the feces, since the calcium forms insoluble salts with the phosphorus and thus absorption is inhibited, while children on a generous flesh diet will excrete most of the phosphorus through the kidneys. The amount excreted through the urine on mother's milk varied from 0.04 to 0.08 gm., while on cow's milk it was much higher, being 0.589 gm. in Blauberg's case and as high as 2.009 gm. in one of my determinations. (See phosphorus tabulations.)

In the feces from mother's milk feedings, the elimination varied from 0.02 gm. to 0.036 gm., while on cow's milk it was 0.962 in Blauberg's case. My own determinations were 0.7648, 0.5991 and 0.3789 gm., the larger quantity appearing with the lower fat-content of feeding and diminishing as the fat was increased.

A number of investigators have tried to show that the elimination of phosphorus and nitrogen was parallel, arguing from the fact that with cell destruction both N and P were released; and, indeed, this is true for certain groups of tissues, and could we estimate their catabolism separately, this would be our result. However, since N is only influenced in the protein wear and tear of the body, and since phosphorus has many influences other than is brought about by its connection with nitrogen in the albuminous molecule, as a number of observers have shown—Ehrstrom, and more recently L. F. Meyer[36]—there may be nitrogen retention with a phosphorus loss, and vice versa. The fact, too, that phosphorus is retained so tenaciously, while nitrogen is more readily given up, is another reason why the ratio of $N:P_2O_5$ in the urine is of little value as an index to cellular metabolism. The phosphorus balance obtained by considering the intake and elimination through feces and urine can only be depended on for correct interpretation of metabolic activity of phosphorus, and, indeed, the same may be held for any of the food constituents.

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36. Meyer, L. F.: Ztschr. f. physiol. Chem., 1904, xliii.

ANOMALIES IN PHOSPHORUS RETENTION

The anomalies related under the head of calcium retention are all shared in by phosphorus. Indeed, the pathologic conditions which affect one nearly always affect the other. As has been stated, in rachitis and osteomalacia there is a disturbance of retention of the phosphorus, particularly that part bound with calcium and magnesium. In these diseases the giving of calcium increases the retention of phosphorus and the giving of phosphorus increases the retention of calcium, proving undoubtedly their chemical and physiologic affinity.

Phosphorus has a close connection with intermediary metabolism, as shown by its large content in the thyroid gland, the ovaries and the testes. So great is the necessity for phosphorus in the functioning of the testes and ovaries that castration is sometimes employed in order to divert the phosphorus to the use of the bones, as has been done occasionally in osteomalacia.

In that anomaly known as phosphaturia, in which the ratio of P_2O_5 to CaO changes from 12:1 to 4:1, if a calcium-poor diet is given, the phosphates quickly disappear. Phosphorus may be retained in abnormally large quantities as pointed out by L. F. Meyer.[37]

SODIUM AND POTASSIUM

The relationship of potassium and sodium to the maintenance of the alkalinity is a very interesting and important one. The study of the influence of their *ions* on muscle-contractility and nervous irritability is yielding valuable data. The power of their *ions* to influence body weight, body temperature, pulse and even leukocyte count is a most important contribution made by L. F. Meyer[37] and S. Cohn.[23]

We will first discuss the problems of alkalinity into which Na and K enter, since these elements form the fixed alkalies. Under the anomalies of alkalinity we will discuss the problems which relate to variations of this alkalinity.

It should be remembered that both alkaline and acid solutions exist within the same body; that the blood, various secretions, as well as each body cell has a definite amount of alkali, and can vary only within very narrow limits in order that they may perform their proper functions. This automatic regulation of alkalinity of the tissues and fluids is one of the marvels of the human mechanism, and it is remarkable how rarely it varies sufficiently to produce a pathologic condition. It is for the maintenance of this stupendously important work that the fixed alkalies, sodium and potassium, are used. Albu and Neuberg[28] have explained this self-regulation thus: Through the tearing down of the albumin of the body and the albumin taken in in the food, sulphuric and phosphoric acids are set free and must be neutralized by the alkalies of the blood. These acids would draw out the fixed alkalies were it not for the supply of carbonate derived from the carbonic acid and from the vegetable salts taken in the food. At certain times when the breaking down of albumin is excessive, ammonia is also set free and this is used along with the carbonates for the fixing of the acids. By means of this sort of neutralization, the acids become a constituent of the body, the fixed alkalies remain untouched, and the alkalinity of the tissues is unchanged. Should this reaction suffer the least change, either through a lessening of the bases or an increase of the autogenous acids, the organism becomes at once in danger.

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[37] Meyer, L. F.: Deutsch. med. Wchnschr., 1905, No. 37.

The constant chemical reaction is also necessary for the ferment action which takes place throughout the body. The alkalies act also as carriers of the carbonic acid in the blood-stream.

The *ions* of potassium and sodium have an important bearing on the heart action, as shown by Overton.[38] K *ions* do not seem an absolutely necessary accompaniment of rhythmical action, but if present in too large numbers they cause a depression, even to complete inhibition. On the other hand, Na *ions* are necessary to contractility and irritability of heart-muscle. If present alone they produce muscular relaxation.

Jacques Loeb[26] has shown how closely developing life is dependent on exact proportions of NaCl in solution as shown by his experiments in sea-water, physiologic salt solution and in water with no NaCl in it.

Let us, therefore, study the sources of supply of these important elements, and see if we can determine the daily need for the growing infant. (See tabulation on page 131.)

In mother's milk there is much less sodium and potassium than in cow's milk. There is more potassium than sodium in each of these milks. The daily need of the nursing infant as represented by the intake is for sodium 0.5877 gm., and for potassium 1.1032 gm. In cow's milk feeding the sodium intake was below the intake on mother's milk and the potassium intake was considerably above that on mother's milk.

ABSORPTION

The absorption is relatively good on both milks. On absorption the Na salt takes its place in the blood and tissue fluids, while the potassium, displaying its selective action, takes its place in the various body-cells and in the blood-cells. Its most common salts are potassium phosphate, which is the chief mineral constituent of red blood corpuscles, and potassium chlorid, which is found in the body-cells. The potassium salts make up 0.4 per cent. of the total blood and 0.65 to 0.8 per cent. of fresh muscle tissue. It is evident therefore that for the production of

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[38] Overton: Arch. f. d. ges. Physiol. Bonn (Pflüger), 1902, xcii, 346.

POTASSIUM AS K_2O

In 1,000 gm. mother's milk 0.69 gm. K_2O.
In 1,000 gm. cow's milk 1.885 gm. K_2O.

Food	Intake	Elimination		Absorption		Retention	
		Feces	Urine	Gm.	Per cent.	Gm.	Per cent.
Mother's milk (Klotz)	1.1032	0.2842	0.1591	....	....	0.6598	74.2
Cow's milk (Meyer)	1.9605	0.2033	1.4411	....	....	0.8161	16.12
Cow's milk (Blauberg)	1.57	0.271	1.12	1.30	82.8	0.180	11.5

Figures given above are in grams in 24 hours.

SODIUM AS Na_2O

In 1,000 gm. mother's milk there is .049 gm. Na_2O.
In 1,000 gm. cow's milk there is .465 gm. Na_2O.

Food	Intake	Elimination		Absorption		Retention	
		Feces	Urine	Gm.	Per cent.	Gm.	Per cent.
Mother's milk	0.5877	0.1924	0.1481	....	....	0.2471	67.2
Cow's milk	0.478	0.075	0.3305	....	....	0.0725	15.27
Cow's milk (Soldner)	0.409	0.098	0.343	.311	75.9	Negative	....

Figures given above are in grams in 24 hours.

the muscle of the growing child an adequate supply of potassium salts must be given.

RETENTION

The retention in per cent. of intake in mother's milk is very good, being 67.0 per cent. for sodium and 74 per cent. for potassium, while the retention on cow's milk is relatively poor, being 15.27 per cent. for sodium and 16.12 per cent. for potassium.

ELIMINATION

K and Na are eliminated through the urine and feces. The potassium in the urine is bound with Cl and with phosphorus and the sodium chiefly as NaCl. The sodium of the urine largely depends on the sodium intake in the food, while the potassium in the urine depends on the destruction of tissue; hence K metabolism is parallel with tissue destruction. This is explained by the fact that K is in the cells and is more closely bound, while Na is held in solution in the blood and tissue fluids and, therefore, more readily excreted. The normal ratio of Na to K in the urine is 3:1, 2:1 and some authors place it as 5:3.

ELIMINATION THROUGH THE FECES

About 15 to 25 per cent. of the intake of K and N are eliminated through the feces. These amounts vary considerably with the kind of diet, whether it is rich in alkali or not, or whether it is vegetable or made up of a considerable part of meat.

ANOMALIES OF RETENTION OF FIXED ALKALI

There is at times an over-retention of potassium salts to the point of potassium intoxication, and some authors[28] have attempted to build a theory for uremia on this fact. In such cases the potassium salts are retained in the blood-stream rather than taking their places in the tissue structure. But the most common anomaly is not that of over-retention but of marked withdrawal of the fixed alkalies. Against such a contingency the organism of the carnivora has builded up a strong resistance. First in the use of the carbonate of the tissue fluids and blood, and, as a last resort, in the production of ammonia. As has been previously stated, under normal conditions the carbonates with the help of a small amount of ammonia, are sufficient to care for the normal production of acids in the body. Under abnormal production of acids, as occurs in diabetes and in conditions of acidosis in certain infants fed on high fat mixtures, and in some older children fed on a mixed diet containing a quart or more of rich milk, there is a demand for a large quantity of ammonia to protect the fixed alkali.

A vast number of researches have been carried on covering the field of conditions of acidosis. It was Salkowski in his experiments on dogs

CHLORIN AS NaCl

In 1,000 gm. mother's milk, 0.294 gm. Cl.
In 1,000 gm. cow's milk, 0.82 gm. Cl.
In 1,000 gm. cow's milk (Hoobler), 1.8678 gm. NaCl.

		Elimination		Absorption			Retention		
Food	Intake	Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	0.3297	0.0135	0.1776	0.3162	95.4	....	0.1386	58.0	....
Diluted cow's milk, 2.1% fat (Hoobler)	2.3178	0.042	2.2421	2.2758	98.1	.274	0.0337	1.4	.004
Whole cow's milk, 4% fat (Hoobler)	2.3926	0.1567	2.3328	2.2359	93.4	.286	Negative	....	....
Cow's milk and cream, 5.4% fat (Hoobler)	2.3428	0.06031	2.1340	2.2824	97.3	.288	0.14849	6.3	.018

Figures given above are in grams in 24 hours.

who first pointed out that the self-produced body acids were bound by the withdrawal of the fixed bases of the body, and thus there would be impoverishment of these indispensable mineral constituents were it not for the fact that the carnivora are protected by this increased ammonia excretion; but this protection is only within narrow limits.

Not only is the withdrawal of alkali accomplished through the overproduction of acids, but it has been shown that a diet rich in fats will cause a withdrawal of alkali for the purpose of combining with the fatty acids of the stools. The fatty acids will first utilize such alkaline earths (Ca and Mg) as are available, and then for further neutralization will call on the fixed alkali of the body. This in turn demands the production of ammonia for the protection of the fixed alkali. This often occurs in healthy infants when on a high fat mixture, but it takes place preeminently, as shown by L. F. Meyer,[23] in the stage of decomposition of Finkelstein's *Ernährungstörung*. In this condition not only does the fat cause loss of alkali, but even sugar produces the same result.

SODIUM CHLORID

Of all the mineral constituents, sodium chlorid has the most varied and important functions to perform. The function of maintaining osmotic pressure has been the one most studied, and its relation to the retention and excretion of water is well known. In recent years to the Na *ions* and the Cl *ions,* acting either separately or in conjunction, have been assigned various results. L. F. Meyer[23] has shown that the intake of Na *ions,* especially when bound with the halogen group, particularly with chlorin, when in certain concentration, viz., 3 gm. NaCl to 100 c.c. water, always produced an increase of temperature in a young infant. There is a marked decrease in the body weight when fed on milk freed of salts; also the pulse and leukocyte count are affected. Just what the daily need of this salt is depends largely on the kind of food ingested. There is a certain demand for this salt and when the intake is cut off the body retains with great tenacity what it has until further intake occurs.

The chlorin intake in mother's milk is 0.3297 gm., while on cow's milk the chlorin intake in terms of NaCl was 2.3926. The tabulation on page 133 shows the chlorin metabolism in terms of NaCl.

The demand for NaCl is greater in herbivora than in carnivora, because of the greater consumption of K carbonates, as was pointed out in the classic observation by Bunge.[39] His concise explanation of this phenomenon is that with a large intake of K carbonate there is formed in the blood the salts of sodium phosphate and potassium chlorid. Both being foreign, they are eliminated, leaving a loss of NaCl which must be replenished.

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[39] Bunge: Cited by Albu and Neuberg, Mineralstoffwechsel, p. 164.

NaCl is ingested in large quantities. It being well absorbed, there is an increased quantity in the blood, hence its isotonicity is disturbed and either there must be a holding back of water until the solution is isotonic, or an increased elimination of the NaCl. Both of these processes may take place.

ABSORPTION

The absorption of salt is found to be excellent—usually above 90 per cent. of the intake is absorbed. The retention of NaCl is only sufficient to cause a balance to be maintained under normal conditions. In my determinations I found that there was utilized but 1.4 per cent. to 6.3 per cent. of the intake.

ELIMINATION

The elimination takes place almost entirely through the kidneys. But a very small quantity appears in the feces, so well is it absorbed. In my determinations there was a little over 2 gm. excreted through the urine daily, while less than 0.1 gm. appeared in the feces.

It has been observed that salt solution when injected subcutaneously is more quickly eliminated than when taken by mouth. With the excretion of NaCl there must accompany it a certain amount of water, and, therefore, the intensity of diuresis depends on the molecular concentration within the body. Not only does salt affect the retention and withdrawal of water, but it holds a very close relation to nitrogen.

Voit's original work seemed to show that with increasing retention of NaCl there was an increased retention of nitrogen; later investigations have not agreed with this. Belli[40] sums up his findings with the statement that in small amounts, as in the food normally, it hastens and increases protein retention, but in greater quantities it tends to lessen the nitrogen retention.

THE ANOMALIES OF NaCl RETENTION

There are a number of conditions which seem markedly affected by sodium chlorid. The most important is that of nephritis. Von Noorden[41] was the first to work on this important condition. He noted a variation in different cases. Some retained and others did not retain NaCl. Halpern[42] has shown that both in acute and chronic nephritis the salt content of the urine is dependent on the salt content of the food. In cases in which there is edema there is marked lessening of the edema when the patient is put on a salt-free diet, and there appears in the urine an increase in the NaCl elimination. The use of salt-free diet, whether with or without edema, brings about more or less of a dechloruration of the body. It would seem that in these cases the NaCl retention always precedes the water retention and that the edema consequent on water retention is due to the NaCl retained. However, no hard and fast rules can be laid down in regard to use of salt-free diet, as in some cases it will not reduce edema, and in some cases a salt-rich diet will not always produce NaCl retention.

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[40] Belli: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 170.

[41] Von Noorden: Lehrbuch d. Pathologie d. Stoffwechsels, Berlin, 1893.

[42] Halpern: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 174.

L. F. Meyer[23] believes that many of the symptoms present in food disturbances of infants may be traced to the deleterious influence of sodium chlorid, acting not only as salt, but also in the capacity of the respective *ions*. He believes particularly that the rises of temperature during the stage of intoxication of Finkelstein's *Ernährungstörung* is due to the action of these *ions*. In children with food disturbances smaller quantities of NaCl solution will raise temperature more quickly than in healthy children.

Fisher[43] has shown that the injection of salt solution of one-sixth molecular strength may produce glycosuria, and that this glycosuria may be stopped by injecting a calcium chlorid solution.

Abderhalden[6] believes that every cell has particular salts in specific apportionment and that a disturbance of this relation, as would take place in Fisher's experiment just quoted, would cause considerable trouble in the life processes of the cell.

SULPHUR

Of all the mineral salts, sulphur has been the last to receive due attention at the hands of investigators. What we know of sulphur metabolism is largely due to Freund[46] and his pupils. Sulphur presents itself for ingestion in the food in two different forms, viz., in the inorganic salts, and organically bound with albumin. The inorganic salts have little or no effect on metabolism and need not be considered. It is that sulphur which is organically bound which is the important part and which supplies the daily need of the growing infant.

Whether or not sulphur is necessary for the maintenance of life is still a question, but any substance so closely associated with nitrogen may be assumed to have a distinct function, though as yet this function is obscure.

The total sulphur intake of infants fed on mother's milk is .04 gm., while on cow's milk the daily intake is about 0.44 gm., according to my recent researches. The sulphur of mother's milk is very well absorbed, as is also that of cow's milk. My determinations show that it is absorbed in from 88.2 to 95.7 per cent. of intake. This absorption is quite in

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[43] Fisher: Cited by Abderhalden, Lehrbuch d. physiolog. Chemie, Berlin. 1909, p. 358.

[46] Freund: Zeit. f. phys. Chem., Strassburg, 1900, xxix, 24-46.

SULPHUR IN TERMS OF S

In 1,000 gm. mother's milk, total sulphur .0572 gm.
In 1,000 gm. cow's milk (Hoobler), total sulphur .33538 gm.

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	.0396	.0096	.026	.0298	75.5	....	.0039	9.8	....
Cow's milk	.5832	.01484	.2019	.0436	74.5	....	Negative	....	....
Diluted cow's milk, 2.1% fat (Hoobler)	.46308	.0542	.3777	.4089	88.2	.491	Negative	....	....
Whole cow's milk, 4% fat (Hoobler)	.4411	.02430	.26589	.4168	94.2	.531	.15091	34.2	.019
Cow's milk and cream, 5.4% fat (Hoobler)	.4444	.01901	.30585	.42546	95.7	.533	.11961	26.9	.015

Figures given above are in grams in 24 hours.

keeping with the facility with which nitrogen is absorbed, and this is probably due to the fact that its connection with the albumin molecule is so close. (See tabulation, page 137.)

The absorption takes place through the small intestine, and some of it is again eliminated into the large intestine, making up the sulphur found in the feces.

Schwarz[47] found in a 5-year-old child on a mixed diet that the absorption was very good, being 92.2 per cent. of the intake. My normal child on a milk diet had an absorption of 92.4 per cent. of the intake. Identical methods of determination were used by both of us.

RETENTION

The retention of sulphur in mother's milk feeding is very good, while with cow's milk the retention is relatively poor. In one of my determinations there was a negative balance and in two others 34.2 and 26.9 per cent. of the intake was retained. Schwarz,[47] in a normal 5-year-old child on a mixed diet found that sulphur retention was relatively poor, being 31.1 per cent. of the intake.

ELIMINATION

The elimination of sulphur occurs mostly through the urine. In cow's milk feeding ten times as much appeared excreted through the urine as through the feces.

The sulphur in the feces appears as iron sulphate and alkali sulphate, while in the urine there are recognized four different forms, viz., the inorganic sulphate sulphur, the ethereal sulphate sulphur, neutral sulphur and basic sulphur. The first named is by far the most abundant in the urine, making up about 80 per cent. of the total sulphur. Ethereal sulphate sulphur makes up about 8 per cent. of the total sulphur and the neutral and basic sulphurs the balance.

Just what significance should be assigned to total sulphur and to each of the various sulphurs making up the total, has been the subject of much speculation.

Because of the connection between sulphur and albumin in tissues, the sulphur metabolism has been taken as the index to protein metabolism. The normal ratio is $N : H_2SO_4 :: 5 : 1$.

The relative amount of ethereal sulphate sulphur has been taken as an index of the degree of albuminous putrefaction going on in the intestine, and also for the breaking down of albuminous cells in the body.

The neutral sulphur appears to be increased on a vegetable diet and decreased on a meat diet. Investigators have shown that in periods of starvation, as well as in other conditions of protein break-down, there is an increase in the per cent. which neutral sulphur holds to total sulphur.

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[47] Schwarz: Jahrb. f. Kinderh., 1910, lxxii, p. 549.

Lepine[48] is the authority for believing that neutral sulphur has its origin partly from the taurin of the bile. This is first excreted into the intestine, reabsorbed, and again eliminated through the urine. In those conditions of disturbed oxidation, if below normal, neutral sulphur is low; if above normal, then the neutral sulphur is increased. In my determinations of neutral sulphur it appears that on cow's milk containing 2.1 per cent. fat the neutral sulphur averaged 7.2 per cent. of the total sulphur, but that on feeding 4 per cent. and 5.4 per cent. fat mixtures the neutral sulphur was increased to as high as 15 per cent., more than doubled. This might be explained by the fact that during these higher fat feedings small amounts of acetone, diacetic acid and beta-oxybutyric acid were found in the urine, forecasting an impending acidosis, in which already tissue albumin had begun to disintegrate.

ANOMALIES OF SULPHUR RETENTION

Schwarz has shown that in rachitis the total sulphur absorption in two cases was 76.9 and 83 per cent., which was somewhat lower than in his normal case, which showed 92.2 per cent. absorption. The retention in one case was 30.9 per cent. and in the other 26.1 per cent. of the intake. This was about the same as in his normal case, viz., 31.1 per cent.

There was eliminated through the urine 55 per cent. of the total sulphur in one case and 54.1 in the other, while in the urine of his normal case 61.1 per cent. was thus eliminated. The elimination by the feces in two of his cases of rachitis showed a marked change from his normal case—23.1 per cent. and 17 per cent. in rachitis and but 7.8 per cent. in the normal.

Of the various forms of sulphur in the urine, the only one which showed much variation from the normal was that of the neutral sulphur, which in two of his cases was considerably increased, being 18.5 per cent. and 18.6 per cent., while his normal showed 7.8 per cent. of the total sulphur. In one of his rachitic cases no variation from the normal occurred.

A further anomaly of sulphur metabolism is that of cystinuria. Bunge has shown that in the catabolism of cystin, albumin, which has sulphur in it, sets sulphur free, which usually unites with bases and is eliminated as sulphates; but if the bases are lacking, then alkali is drawn from the cells of the body.

SUMMARY

1. Salts are necessary to maintain life.
2. Salts are best absorbed and utilized when in organic combination with food stuffs.

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[48] Lepine: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 148.

3. There are marked differences in the salt content of mother's and cow's milk which should be considered in artificial feeding.

4. Certain pathologic conditions arise in which certain of the salts are not absorbed, even though in abundance in the food.

5. In certain other pathologic conditions salts are actually withdrawn from the body to such an extent as to impoverish the organism and produce grave disturbances of nutrition.

6. The various salts, with the exception of iron, are present in sufficient quantities and proper proportions in mother's milk. In most of the dilutions of cow's milk there is an excess of salts which may be neglected in feeding normal infants, but which plays an important rôle in the feeding of children already suffering from nutritional disturbances. The conditions under which the salt content of feedings should be altered and in just what degree each or all should be varied, are still unsolved problems.

131 East Sixty-Seventh Street.

PROGRESS IN PEDIATRICS

ACUTE INFECTIOUS DISEASES

Poliomyelitis

The unfailing regularity with which the United States has been visited by epidemic poliomyelitis makes it insistent that every practitioner in the country should be conversant with the progress of knowledge in regard to this malady.

In the past four years it has become widely distributed. Its ravages have extended completely across the continent; but few of the Southern States, even, having been free from the scourge.

Before 1907 the most clearly defined focus of the disease was in Scandinavia, and the first point affected by poliomyelitis in this country was the part of the Middle West in which a large settlement of Scandinavians had formed.

According to the information procured during the Scandinavian epidemics, it would appear that the contagion can be carried from the ill to the well by intermediate agencies. The incubation period is variable, but the mean is about ten days in length—a space of time equal to that required for the journey from affected districts in Europe to the United States.

These, and certain other equally suggestive circumstances, have led to a widespread renewal of interest in the epidemiology of the disease.

Experiment, and the observation of large numbers of cases, have of late helped us vastly to an accurate conception of processes which only a few years ago were subjects of the vaguest surmise. Unfortunately we cannot as yet point definitely to any precise method of prevention; nor yet even to a method whereby the severity of an epidemic already existing may be diminished; nor yet, again, are we in a position to be able unfailingly to abort the progress of these pathologic conditions in individual cases. However, the sum of knowledge has in the past three years been enormously augmented, and it must be a source of satisfaction to every American that the credit for these advances is mainly due to workers in American hospitals and laboratories.

An attempt will now be made to sketch as briefly as may be an outline of the more important of these results.

In the summer of 1909 Landsteiner and Popper succeeded in producing the disease in two monkeys by intraperitoneal injection of the emulsified spinal cord obtained from a fatal case of poliomyelitis. They failed, however, to transmit the disease from these to other monkeys.

In September of the same year Lewis and Flexner in this country also succeeded in producing the disease in monkeys by means of intracerebral injection of poliomyelitic cord. The cords of the affected monkeys furnished a virus to these observers which, by September, 1910, they had propagated through twenty-five separate series of monkeys.

The incubation period was taken to be the length of time between the date of inoculation and the first appearance of definite paralysis; this was of variable length, but the average corresponded to the ten days already surmised to be the incubation period in human poliomyelitis. In the early part of this period the animals showed no sign of ill-health, but from six to forty-eight hours before the onset of paralysis they became nervous and excitable, and easily tired. Their gaze became shifting rather than fixed, as it is in the normal animal. The temperature was not much raised and gastro-intestinal symptoms were infrequent.

These somewhat vague prodromal signs were followed by the onset of paralysis. the distribution of which corresponded almost precisely with that found when the disease occurs spontaneously in man.

The inoculated disease in monkeys differs markedly in its mortality from the human affection. At least half of the animals inoculated died, whereas the fatal cases in human poliomyelitis do not exceed 10 per cent. of those attacked even in the most severe epidemics. But it might here be suggested that the notorious delicacy of the monkey, especially in captivity, is sufficient completely to remove this single discrepancy between the human and experimental conditions.

The lesions produced in the central nervous system in both the spontaneous and experimental diseases are almost exactly similar.

The microscopic lesions in the brains and cords of monkeys dying of the disease consisted mainly of congestion and hemorrhages into the gray matter; the anterior horns being disproportionately affected. The entire spinal cord was involved in a series of wide-spread vascular accidents, the cord injury, however, corresponding in position to the greater palsies of muscle groups.

The lesions consisted of a small round-celled infiltration in the perivascular spaces with the development of considerable edema. Arterial thrombosis was never apparent, and the degeneration and necrosis of cells was invariably produced by gross pressure of inflammatory exudates on the cells and the nutrient blood-vessels. A leptomeningeal infiltration of mononuclear cells was always present and was perivascular in position.

The greater affection of the anterior over the posterior horns is explicable by the richness of the vascular supply to the former; a similar consideration serves to explain the apparently disproportionate involvement of the lumbar and cervical enlargements.

The organism of poliomyelitis belongs to the class of filtrable viruses; its potency is not reduced by being passed through a Chamberland filter. The clear fluid obtained by filtration of poliomyelitic cords has been seen to contain innumerable bright, dancing spots when examined under the dark field microscope; these points were not found in filtrates similarly obtained from normal cords; it remains to be seen whether or not they represent the organism of the disease.

It is doubtful if the virus can be grown in culture media. It withstands glycerinization, drying, and freezing over prolonged periods, but is readily destroyed by heat, and by comparatively weak antiseptics, such as menthol, and a 1 per cent. solution of hydrogen peroxid.

The virus is contained in the brain, spinal cord, lymphatic glands, salivary glands and nasal mucosa. At the beginning of the infection the blood and cerebrospinal fluid have also been found, sometimes, to be capable of producing the disease when injected into a suitable host.

It can be inoculated with success into the brain; into the subdural space; subcutaneously. Infection has been produced by the introduction of toxic filtrate into the stomach by means of a catheter, and by injection into the intestines; a necessary condition, however, being the previous exhibition of opium to restrain peristalsis. The disease has also been caused by rubbing the nasal mucous membranes with a toxic suspension, though for certain success, previous scarification of the nasal mucosa is required. A similar proviso applies to infection *via* the trachea and the rest of the respiratory tract.

Attempts to inoculate the disease in monkeys which had been already attacked were invariably unsuccessful. Further, the serum of both monkeys and human beings recently recovered has been found to possess the power of diminishing, or occasionally completely neutralizing the virus *in vitro,* and in the bodies of infected monkeys.

If hexamethylenamin (urotropin) be administered to a monkey, it is excreted into the cerebrospinal fluid. If, then, that monkey be inoculated, the incubation period will be frequently prolonged, and the severity of the attack diminished. Further, if in addition to the administration of hexamethylenamin, the animal be injected with immune monkey-serum, the onset of paralysis is most often entirely prevented.

Kraus has recently shown that the injection of 10 c.c. of poliomyelitis virus, sterilized by being treated with 1.5 per cent. phenol, completely protects the macacus against subsequent inoculation of active virus, an observation which, if confirmed for man, opens up the possibility of successful vaccination against this disease.

The active immunity conferred by an attack of poliomyelitis obtains, apparently, for a period of at least three years. Active immunization of monkeys has been achieved by the repeated inoculation of small doses of virus over a period of several months, after which an inoculation of maximum potency was harmless. Previous glycerinization of the virus apparently renders it more suitable for immunizing purposes.

In the attempt to obtain an artificial antiserum it has been found that the normal sheep-serum has the power definitely to diminish the potency of the filtered virus; and if the sheep be previously injected with immune monkey-serum this neutralizing property becomes markedly augmented.

It must, however, be pointed out that the endeavor to produce an entirely satisfactory antiserum has not as yet met with success; that much experimentation must still be completed; and that the ideal antiserum, when obtained, will have to be employed in the very beginning of the disease before any lesion of the central nervous system has yet occurred—a condition which makes it necessary for us to achieve more exact methods of diagnosis in the prodromal period of the condition.

The symptomatology of the disease is so well known that it seems almost unnecessary to dwell long on this section of the subject.

The eight classes to which Wickman drew attention may be mentioned:

1. Spinal poliomyelitis form—a sudden feverish attack followed by the palsy of one or more limbs.

2. An ascending form in which, first, are involved the legs, and later the muscles of the abdomen and thorax. This type is often fatal.

3. A bulbar type, with palsies of the various pontine and medullary cranial nerve nuclei.

4. Polio-encephalitis, from which a state of meningismus with spastic paralyses may ensue. Koplik, in a notable paper in the *American Journal of Medical Sciences* has done much clearly to depict the clinical picture presented by this condition.

5. Ataxic polio-encephalitis, by which is merely meant an inflammatory process, the maximum stress of which falls on the cerebellum. The clinical symptoms are briefly, an acute illness of short duration, followed by motor ataxia of the arms and legs, nystagmus and explosive syllabic speech. The writer has not been able to find statistics on the frequency of occurrence of this form of the disease, but his impression has been that it occurs in adults more frequently than do other types of the affection.

6. The polyneuritic form; practically impossible to diagnose as a distinct entity, but its existence has been proved by autopsy.

7. The meningitic form. Since Wickman's formulation our knowledge has been advanced sufficiently to show us that practically in all cases the meninges are very markedly affected. Clinical and pathologic studies combine to make it needless to classify separately this condition.

8. Abortive forms in which only general constitutional disturbances occur, and paralyses are either quite fleeting, or entirely absent. The correct diagnosis in these cases can only be surmised from the co-existence of an epidemic of the disease, though possibly assistance may be obtained from the picture presented by the blood and cerebrospinal fluid.

Experimental studies by Flexner and Lewis show that in the preparalytic stages the cerebrospinal fluid exhibits definite evidences of the round-celled infiltration of the meninges to which references have already been made. Within forty-eight hours of inoculation the fluid is found to be under increased pressure;

a little later it contains an increased number of lymphocytes which give it an opalescent appearance; its coagulability is also greatly increased. These changes have disappeared by the time definite palsies have developed.

These facts, coupled with Muller's observations, confirmed by many observers, that in the initial febrile period there are leukopenia, profuse sweating and intense hyperesthesia, give us some hope, but no certainty, of being able to recognize the early stages of the disease by the time the laboratory workers put weapons into our hands.

The fact that the mucous membrane and salivary glands of infected monkeys have been shown to be potent to reproduce the disease, would appear to justify us in supposing the secretions of these to be infective; the cribriform plate offers the most convenient avenue for the passage of organisms between the meninges and the external world, a consideration which must be borne in mind when we come to draw up preventive measures.

It is certain that the period in which epidemic poliomyelitis is most violent includes the warm, dry months of August and September; it is not clear that density of population is any factor in the proportionate severity of any particular epidemic, and the problem of the method by which the disease frequently is transmitted in little populated and extensive districts, is one difficult of solution.

A notable contribution to the clearing up of this question was lately made by workers in the Rockefeller Institute, who succeeded in producing the disease in monkeys by the intracerebral injection of an emulsion, made from the bodies of common house-flies, which had been fed on portions of spinal cord obtained from a poliomyelitic monkey.

The direct contagiousness of poliomyelitis is exceedingly slight; true, many times two or three cases have occurred in one family, but the transmission of the disease from one patient to another has been difficult of proof, and the sporadic and apparently well-isolated cases far out-number those in which infection could be argued for with any conviction; the spread of an epidemic seems to be independent, too, of poisoned food or water-supply, though the general direction is usually along low-lying parts of the country, and especially along those in which water areas exist.

The trend of all these considerations would seem to indicate the transmission of the disease, not by contact or infection as in measles or scarlet fever, not by ingestion of toxic material, but rather by the intermediate agency of insects; for detail in this theory—or for its condemnation—further experiment must be awaited.

All authorities demand strongly, however, that the disease be made universally reportable, and it is to be hoped that legislation to this effect will speedily be achieved.

In view of our yet nebulous knowledge as to the transmissibility and contagiousness of the condition, all cases should be isolated, and it would be well to insist that the same precautions be observed as would be applicable in a case of scarlet fever.

In addition to these precautions, particular care should be taken to disinfect the nasal and pharyngeal passages by means of the frequent use of a spray of 1 per cent. solution of hydrogen peroxid. In February of the present year it was proved that the nasal mucous membrane may remain infective for some five or six months, so it would appear that this antiseptic treatment should be extended for a time considerably longer than the duration of acute symptoms.

As a prophylactic measure the routine use of hydrogen peroxid on the part of those living in the neighborhood of infection should be encouraged.

The results of insect experimentation indicate the necessity of the inauguration of a campaign against the common house-fly. Perhaps it is not too much to suggest that united action against this pest might result in beneficial effects to the public health in more directions than that with which this paper more particularly deals.

Foster Kennedy.

NOTICE

Circular issued by the American Orthopedic Association and the American Pediatric Society in reference to acute epidemic poliomyelitis, addressed to health authorities and boards of health.

Anterior poliomyelitis is, so far as known, a communicable disease, being communicated from one patient to another and also by means of a third person. It occurs in epidemics and tends to spread along the lines of greatest travel. There is reason to believe that it is prevented from spreading by quarantine, and with the very great prevalence of the disease in the summer of 1910 it is the opinion of this committee that it is essential that it should be made a reportable disease in all states in order that its presence may be detected and its spread guarded against.

Of particular significance are the so-called abortive cases, in which indefinite ailments occur in children in communities where frank paralysis also exists. These abortive cases of infantile paralysis are undoubtedly a source of infection, and their record and study is of much importance. In a community where cases of infantile paralysis occur, cases of illness with sudden onset of fever and meningeal symptoms should be closely watched and regarded as possibly infectious. In such cases even recovery without paralysis does not establish the fact that the case was not abortive infantile paralysis.

All cases of infantile paralysis should be strictly quarantined, sputum, urine and feces being disinfected, and the same rigid precautions should be adopted as in scarlet fever. This quarantine should, in the opinion of the committee, last for four weeks, in the absence of definite knowledge as to when the infection ends. Children from infected families should not be allowed to go to school until the quarantine is abandoned. The transportation or transfer of acute cases in public conveyances should be strictly forbidden. It would be very desirable to adopt provisional quarantine measures in suspicious cases in a community in which an epidemic prevails.

The report of all cases of infantile paralysis to the public health authorities should be enforced by law, and all deaths from this cause should be properly described and registered. A careful study of epidemics by public health authorities is strongly advised.

Robert W. Lovett, M.D., Chairman.
Henry Koplik, M.D.
H. Winnett Orr, M.D.
Irving M. Snow, M.D., Secretary.

The Rockefeller Institute for Medical Research of New York City announces that it will devote its resources very largely during the present season to the study of anterior poliomyelitis (infantile paralysis) and to the treatment of acute cases of this disease in its hospital. Physicians and health officers desiring to co-operate in this investigation may do so by sending information concerning the occurrence and prevalence of this disease, or by referring acute cases to the Hospital of the Rockefeller Institute. Dr. Flexner renews his request of last year that whenever possible a portion of the spinal cord and of the nasopharyngeal mucosa derived from fatal cases of the disease be sent to him. Specimens should be preserved in glycerin and sent by mail to Simon Flexner, M.D., Sixty-Sixth Street and Avenue A, New York City.

The Occurrence of Infantile Paralysis in Massachusetts in 1910

(*R. W. Lovett, P. A. E. Sheppard: Boston Med. and Surg. Jour., 1911, clxiv, 737*)

Three classes of cases are reported on. 1. The total number reported by physicians—845. 2. The number for which blanks were filled out—601. 3. A group carefully studied by investigators of the board—200. A study of the rainfall for the last ten years shows that during the last four years, when the disease has been carefully studied the driest years have not been attended by the largest number of cases. In 1910 the month with the least rainfall and the highest mean temperature (August) also had the largest number of cases. An investigation of the nearness of the affected houses to railroad or highroad or to water showed no predominating number close to any. Nothing could be found in the age of the house, its sanitary condition, the water-supply, or sewage disposal which might be assigned as a possible cause. Measurement of the amount of dust is inaccurate, but 316 out of 601 streets are reported as having "no treatment." Study of the prevalence of insects must be made on the spot by a person skilled in entomology. Thirty-four homes out of 110 had illness, paralysis or death in eighty-two animals near the time of the human paralysis. The apparent partial immunity of the colored race may be less true than has been supposed. In Springfield there was in incidence of 3.09 per 1,000 among the colored and 1.99 per 1,000 among the white population. In 200 cases carefully studied there was certain direct contact with acute cases in thirty-two cases, indirect contact in ten and direct contact with a possible abortive case in four. Investigations concerning the diet were not of especial interest. Just previous or some time before the attack 60 per cent. of patients had some abnormal condition—malaise, gastro-intestinal or respiratory disturbances. Study of recent illnesses in the same family showed nothing of importance. During the attack 75 per cent. showed some digestive disturbance. Pain and tenderness occurred in 469 out of 601 cases, lasting most commonly one to three weeks. The paralysis nearly always developed within one week after the onset of fever. The back, abdomen, neck and face are frequently involved. Out of 200 patients, 13.5 per cent had entirely recovered at the end of six months. RICHARD M. SMITH.

METABOLISM AND NUTRITION

Determination of Casein in the Curd of Infant Stools by Biologic Methods, Especially Anaphylaxis

(*A. Uffenheimer and Y. Takeno: Ztschr. f. Kinderh., ii, No. 1, p. 32*)

It is held by the authors that when the present day pediatrician speaks of casein curds he refers to something which really does not contain casein. The curds to which they refer in their article are those which are found frequently in the feces of nurslings and which vary in size between that of a pinhead and a pea. They are not the same bodies of which Selter and Talbot have written. These, it is held, possess certain peculiarities and are also found in the stools of children suffering from some digestive disturbance. The present paper details the work done with a view to determining the composition and nature of these curds. First they attempted to use the precipitation method of Hamburger and Knoepfelmacher by means of cow-lactoserum. However, it did not prove practicable and therefore the anaphylactic method was resorted to. The guinea-pig was used and horse serum was injected. The curds were obtained from a large number of diapers, irrespective of the particular sort of food which the children had been taking; in fact, the authors had no knowledge on the subject whatever. Guinea-pigs were injected with the material obtained, some of them intravenously and others subcutaneously. Curds were obtained from twenty-four children. Twenty-two of these were fed on various dilutions of cow's milk. In the case of nine of these the presence of casein was determined by the anaphylactic method twenty-six times. In the case of three children fed on mother's milk, the result was always negative. It was specially interesting that in the case of one infant on whom five examinations were made during the time he was fed on cow's milk, casein was invariably found present in the curd. The positive findings obtained when the curds were treated with a decinormal caustic soda solution convinced the authors that the casein was not denatured. They injected small quantities of a caustic soda casein solution and then followed with an injection of 4 c.c. of a diluted milk solution. In one case severe shock occurred and death in three minutes; in another, extreme emphysema, rapid heart beat, etc.; and in another, severe general disturbances with temperature reduction to 33.2 C. In the next experiments the authors first injected the diluted milk solution and then the curd mixture. The sensibilatrice was the caustic soda casein or the diluted milk solution and the anaphylactic test was made with the curds which it was previously determined contained casein. Four out of five of the experiments were positive. Twenty-one precipitation tests were made with dilutions of lactoserum varying from 1 to 100 and from 1 to 1,000. The result was a negative one in every instance except two. These two examinations were made of the stool of the same child and in each case there was a slight precipitation. Subsequently, forty-four further examinations were made with a better lactoserum than was used in the first instance, the dilution being 1 to 3,000. Of the fourteen children examined seventeen positive results were obtained in five of them. The authors believe that both methods have given the same results, although they prefer the anaphylactic method because of its greater accuracy. They believe that their experiments prove conclusively that the curds found in the stools of sick nurslings fed on cow's milk very often contain casein. They raise the question, however, whether this casein is unchanged casein or para-casein, and they ask again if this substance reacts in the same manner as native casein. F. C. Z.

Nutrition and Growth

(*Hans Aron, Philippine Jour. of Sc., 1911, vi, 1*)

The relationship between nutrition and growth was made the subject of a very exhaustive experimental study by Aron. He made four sets of experiments on fourteen dogs, and noted (1) the influence of a restricted diet on growing dogs; (2) effect on the weight and appearance of the animals; (3) relative amount of change in certain parts of the body as compared with other parts; (4) changes in the chemical constitution of the body; (5) energy requirement and food consumption. Then he studied (1) the biologic considerations concerning the suppression of growth by restricting the food; (2) energy required during growth, and (3) the increase in weight as an index to growth, with special reference to children. The most important results of his experiments may be summarized as follows: A growing animal which receives only sufficient food to keep its body weight constant, or to allow a slight increase, is in a condition of severe starvation. If by a restriction of food the increase in weight is inhibited, the skeleton grows at the expense of other parts of the body, especially of the flesh. Most of the organs retain their weight and size, while the brain grows to reach its normal weight. The composition of the body, when at a constant weight, undergoes remarkable changes: Fat is consumed more or less entirely, the quantity of protein, especially of the muscles, but not of the organs, is diminished and a great proportion of the body tissues is replaced by water; thus, this water and the increase of the skeleton together, replace the body materials lost. The caloric value of 1 gm. body weight of an animal which has undergone such a process to its extreme limit may amount to only one-third of the normal value. It is possible by supplying suitable amounts of food to maintain a dog in an emaciated condition, apparently in good health, and at the weight of a puppy, for nearly one year, while its weight at the end of the year should be three times as great. If such an animal is thereupon fed amply, it fattens and rounds out, but does not reach the size of a control animal which from the beginning has been normally fed. It is unable to make good the growth suspended by the long restriction of food. The growth principally depends on the tendency to grow possessed by the skeleton. The skeleton loses its capability of growing in more advanced age regardless of the size which the animal has reached.

F. C. Z.

American Journal of Diseases of Children

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A CASE OF SCAPHOCEPHALUS WITH RETINAL CHANGES*

ARTHUR WILLARD FAIRBANKS, M.D.
BOSTON

This paper is presented for several reasons, among which are the following:

1. It concerns an interesting and not very common malformation of the cranium.

2. This cranial malformation is associated with certain phenomena which are so distinctive, and so suggestive of serious organic disease, that they entirely distract the attention from the conformation of the skull as a condition of any importance in the symptom-complex, whereas the truth is that the complex of phenomena will never be correctly interpreted unless the cranial malformation *is* considered.

3. In fifteen years' constant handling of large numbers of children, and during the past seven years, especially, congenitally defective children, the case here reported is the first instance of the kind that I have seen.

4. Both myself and a colleague, who has had a great experience with defective children, were completely baffled by the case for several weeks; and finally the fact that I am fortunate enough to be able to report an instance of this condition is of course the immediate incentive of my paper.

It is my duty here to say we are indebted to our former assistant at the City Hospital Clinic, Dr. Abraham Myerson, now of St. Louis, for whatever of interest or profit may be found in the case, for it was he who came across, in the literature, Merle's[1] article that solved the diagnosis of this boy's condition.

It will perhaps be of interest to give this boy's history as it was given to us:

History.—Boy, aged 8; father, mother, a brother and three sisters are normal. Six weeks previous to examination he is said to have had a "cold" with cough, headache and vomiting. When the cold improved the headache and vomiting persisted, the headache being at times extremely severe, and at these times he complained of seeing double. He also complained of being very dizzy. The headache occurred almost daily, with only an occasional day of freedom. He never had a headache previous to the onset of the cold. He never had any difficulty at school, and was in the fourth grade. He was referred to the department of nervous diseases of the City Hospital by the eye department with a statement that he had choked disk, double optic neuritis and double retinal hemorrhage.

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*From the Department for Nervous Diseases, Boston City Hospital.

*Presented before the New England Pediatric Society, March 25, 1911.

[1] Merle: Nouv. iconog. de la Salpêtriere, 1908, xxi, 349.

Examination.—Our examination showed a bright intelligent boy without anatomic stigmata with the exception of a very long, dolichocephalic head, with a very high vault, along the crest of which is a suggestion of a ridge.

Antero-posterior diameter: 21.7. Cephalic Index 58.
Bi-parietal diameter: 12.6.
Circumference: 56.5.
Glabella to inion: 41.0.
Ear to ear: 32.5.
See outlines and photographs Figs. 1 to 5.

External ocular condition apparently normal; no nystagmus; pupils equal and react normally; gait and station normal; no staggering; no tremor, ataxia, asynergia, or paresis; no abnormality or inequality of the reflexes.

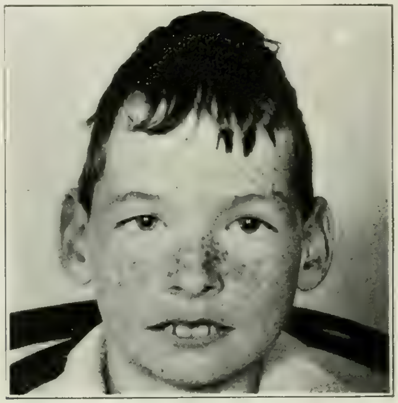


Fig. 1.—Front view of patient showing height of cranium above the ears.

He was referred to the hospital ward for observation for two weeks. There, occasional headache, vomiting and considerable vertigo, persisted for some days, and then gradually subsided, and he was discharged. A week after his return home headache and vertigo again ensued, and moderate Romberg's sign was present.

During the following six weeks he had occasional attacks of vomiting and headache without other definite signs. It was thought at one time that there was slight left internal strabismus, but this was never seen at any other time. Then for four days he had almost constant severe headache and vomiting, but without the former vertigo. A week later his condition was such that his parents requested his admittance to the wards. While in the hospital he had no attacks during the eleven days he was under observation. Ten days later, however, he complained of a blur in his eyes and that he saw things double. Eye examination showed two mm. swelling of the disk and beginning signs of organization. On this occasion and several times previously it was thought that there was slightly less coordination and power in the right upper extremity than in the left, but this was always questionable. No other signs were present. His gait, even with his eyes closed, was excellent. From this time to the time of making this report (six months), he was perfectly well subjectively, and presented no abnormality, except the cranial deformity and the changes in the retina.

As will be seen, the symptoms strongly point to an intracranial tumor. In fact we have the classic general symptoms presenting themselves in a strikingly typical manner—headache, vomiting, optic neuritis, and choked disks, with retinal hemorrhage. When we have said that we have here all the typical so-called general phenomena, we complete the statement as far as any indication of intracranial tumor in this boy is concerned, for we have no focal symptoms. When we remember, however, how long focal signs may be absent in cases of tumor, and when we think of how absolutely typical of intracranial tumor the symptoms, as presented by this child, have always been considered, it is not surprising to know that they were so regarded in this case for many weeks, and only the intermission of the headache and vomiting, and the apparent well-being of the child otherwise, prevented a decompression operation. The symptoms were so intense that the child was twice admitted to the hospital with a view to such radical palliative procedure. The abnormal shape of the head was, of course, noticed, but was thought to be a congenital deformity, without connection with the active and serious clinical phenomena.

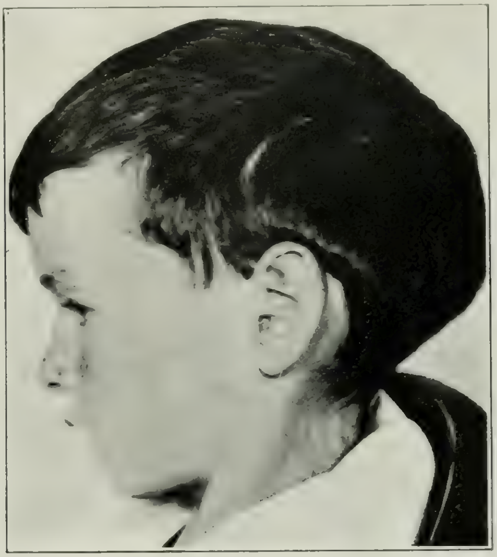
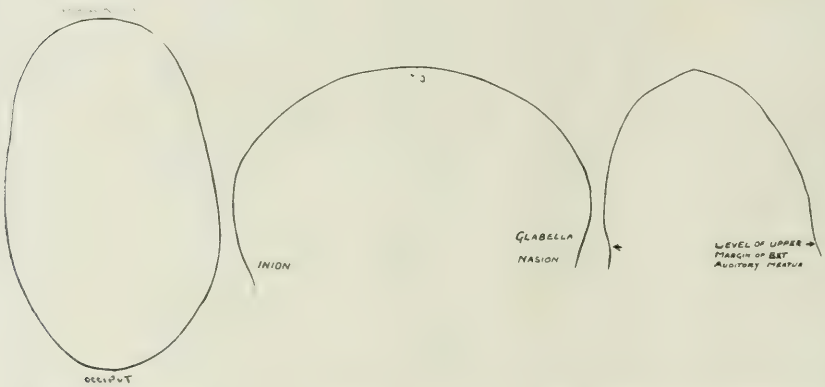


Fig. 2.—Lateral view of patient.

In considering these cases we must start with the basic principle that the variation of the cranium from the normal type is the primary and essential condition, to which all the other phenomena are secondary. We must also recognize the fact that the type of cranial deformity is not always the same. We must keep constantly in mind that the important clinical condition is not the shape of the skull, but the disturbance of function produced by the deformity. We find by a study of the cases reported that in nearly all those instances in which the disturbance of function was present there has been one feature of the cranial configuration that has been practically always conspicuous, and this is the marked increase in the vertical dimension of the cranial vault. The circumference, the anteroposterior and the biparietal diameters all vary widely, and the skull may even be very symmetrical, but the increase in the vertical depth is practically always present, although its degree varies considerably. This, then, appears to be the *essential* element as far as the cranium is concerned.

It is, therefore, incorrect to classify these cases under any such restricted terms as oxycephalus or acrocephalus. By these terms we mean a skull with a more or less pointed vertex. We find, however, that the clinical condition we are considering occurs in a typical manner in individuals with well rounded vertices, and, in rare instances, even in cases in which the vertex is somewhat depressed, the so-called clinocephalus, and we see it in this boy, whose cranium, viewed from the side, is not oxy- or acrocephalic, but more of the scaphocephalic form. But in all of these forms the vertical depth, as a whole, is increased. This is the essential characteristic.



Figs. 3, 4 and 5.—Outlines of skull, around base, over vertex from glabella to inion and over vertex from ear to ear.

I believe, therefore, that this condition should not be classified according to the anthropologic variety of cranium, but rather it should be kept in mind that the condition is merely secondary to the effort of the skull to adapt itself to the growth of the underlying brain, against the handicap of more or less unyielding sutures; and that the three sutures concerned, the coronal, the sagittal and the lambdoid, vary in different cases in their relative rigidity; i. e., in the degree to which they are individually prematurely ossified, thus determining the particular type of skull resulting. A moment's thought will make it clear that if a given suture becomes obliterated the expansion of the cranium in the neighborhood of that suture and in the direction at a right angle horizontally to the course of that suture, will be greatly retarded, if not entirely prevented, and that consequently the skull must expand in other directions to a greater extent than usual to meet the demands of the developing brain.

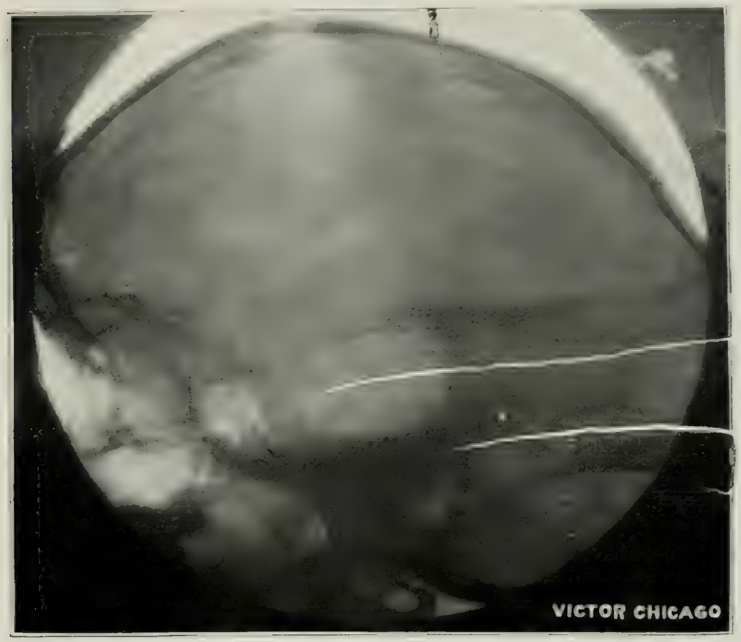
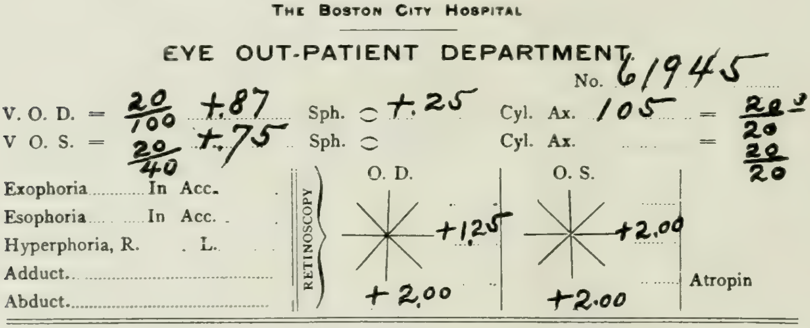


Fig. 6.—Radiograph of cranium showing synostosis of sutures.

Let us suppose, for instance, that the coronal and the lambdoid sutures are the site of premature synostosis. The skull cannot sufficiently increase its anteroposterior diameter. Compensation must be found in an increase in breadth and a lifting of the vertex as a whole. This is achieved by an increased yielding at the sagittal suture with resultant broadening of the cranium, and at the squamous suture, with consequent lifting of the whole cranial vault. Under these circumstances we have formed the true *"Thurmschaedel"* of the German writers. This is an abnormally high but brachycephalic skull. If the three vertical sutures are all prematurely synostosed we have the same lack of development anteroposteriorly as is described above, due to the fixation at the coronal and lambdoid; but in addition we have inability to increase the cranial *breadth*, due to rigidity at the sagittal suture. This means that the increase in capacity of the intracranial space can only take place by a raising of the more or less pointed vertex, and we have as a result the real oxycephalic or acrocephalic skull, the *"Spitzkopf,"* as the Germans term it.

Let us now see what the cranial form would be if the sagittal suture alone were synostosed. Here we have an inability of the cranium to yield to lateral pressure, but comparative freedom to develop anteroposteriorly, and to rise in height. It is obvious that the result would be a long, high cranium with a somewhat sharpened anteroposterior ridge, along the vertex. This is the scaphocephalic skull, of unusual height. This is what we see approximated in the boy whose case is reported. His case, therefore, I believe is due to premature synostosis of the sagittal suture.[2]



THE BOSTON CITY HOSPITAL

EYE OUT-PATIENT DEPARTMENT

No. 61945

V. O. D. = 20/100 +.87 Sph. ○ +.25 Cyl. Ax. 105 = 20/20 3
V O. S. = 20/40 +.75 Sph. ○ Cyl. Ax. = 20/20

Exophoria In Acc.
Esophoria In Acc.
Hyperphoria, R. L.
Adduct.
Abduct.

RETINOSCOPY

O. D. +1.25 +2.00

O. S. +2.00 +2.00

Atropin

Fig. 7.—Chart showing vision and required correction; also showing retinal changes. There is no change in muscle balance.

So much for the formation of these various types of crania. It will be noticed that in all these types the one unvarying characteristic is an increase in the height of the vertex. This accession in height is, as said, compensatory in character, and is rendered possible by continued unrestricted growth along the squamous sutures.

We come now to the most interesting features of these cases, namely, the eye changes (Figs. 7 and 8). The most characteristic, because the most common phenomenon, is the condition revealed to us by the ophthalmoscope.

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[2] Since this opinion was written the accompanying radiograph has been obtained. It shows in superb manner the persistence of the lambdoid, and less clearly the vertical portion of the coronal sutures; while the sagital suture is seen to be completely synostosed. Incidentally the convolutions of the underlying brain show unusually well, proving that the skull, as a whole, is not thickened. This is, I believe, the first instance of the kind in which the condition of the cranial sutures has been actually proved during life.

Optic neuritis in all its stages, choked disk, and post-neuritic optic atrophy, are the features that remove the condition from the realm of anthropology and place it in the domain of clinical medicine. With this syndrome are occasionally seen exophthalmos and deviation of the ocular axes, the latter being practically invariably outward. The last two symptoms are due to changes in the directions of the planes of the orbital walls, resulting in a shortening in length and diminution in capacity of the orbital cavity. It, like the changes in the cranial vault, is compensatory in nature, the direct result of the demand from within the cranial cavity for more room. It is present in some degree in perhaps half of all cases. It has been reported in one or two instances in which the optic nerves and disks showed no evidence of involvement. The external ocular muscles themselves are never paralyzed.

Concentric diminution of the visual fields (Fig. 8) is usually more or less pronounced, especially in the later years, as would be expected. Loss of central vision, without implication of the periphery, is never seen. Two cases[3, 4] are on record in which the restriction of the fields is said to have been nasal, and one with eccentric limitation.[5] It is important to note that the subjective impairment of vision is not always in direct ratio to the severity of the changes revealed by the ophthalmoscope. The amount of vision is often surprising when compared with the condition of the nerve.

The degree of impairment of vision seems to remain fairly stationary when once the neuritis has run its course. All degrees of impairment, from absolute blindness to slight amblyopia, may eventually remain, and

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[3] Michel: Arch. f. Ophth. (Von Graefe). 1866. ii. 133; Fraenkel: Ueber Schädelsynostosen. Arch. f. path. Anat. (Virchow). 1870. l. 145; Michel: Arch. d. Heilk., 1873, xiv, 39; Handb. d. Kinderh. (Gerhardt), v, 515; Zuckerkandl: Mittheil. d. Anthrop. Gesellsch., Wien, July, 1874; Schüller: Centralbl. f. Augenh., 1881, 236; Hirschberg: Centralbl. f. Augenh., 1883, 1; Vossius: Klin. Monatschr. f. Augenh., 1884, 172; Stood: Monatsbl. f. Augenh., 1884, 248; Fridolin: Frühzeitige Schädeldeformität, Arch. f. path. Anat. (Virchow), 1885, 100-266.

[4] Ponfick: Breslau ärztl. Ztschr., 1886, No. 21; Manx: Bull. d. Ophth. Gesellsch., Heidelberg, 1887, 18; Friedenwald: Am. Jour. Med. Sc., 1893, 529; Centralbl. f. Augenh., 1893, 200; Weiss-Brugger: Arch. f. Augenh., 1894, xxviii; Arch. Ophth., 1895, xxiv, 55; Hanotte: Anatomie pathol. de l'oxycephales: Thèse de Paris, 1898; Atgier: Bull. de la Soc. d'anthrop. de Paris, ii, Series 5, 1901; Friedenwald: Arch. Ophth., 1901, xxx, 405; Vortisch: Ueber Sehnervenerkrank. bei Turmschädel, Inaug. Dissert., Tübingen, 1901.

[5] Oliver: Proc. Am. Philosoph. Soc., 1902, xli; Kraus: Zur Kasuistik der Sehnervenleiden bei Schädelmissbildung, Inaug. Dissert., Giessen, 1902; Enslin: Arch. f. Ophth. (Von Graefe), 1904, lviii, 151; Patry: Ann. d'ocul., 1905, 249; Meltzer: Neurol. Centralbl., 1908, 562; München. med. Wchnschr., 1908, ii, 2060.

it may be very unequal in the two eyes. Retinal hemorrhages occurred in my patient, and also in a patient seen by Hirschberg.[5] Nystagmus has been reported, but it is so inconstant as hardly to justify its inclusion in the typical picture of the condition. It is always double and always when it occurs it is seen in cases with marked diminution of visual power. The palpebral fissure is occasionally somewhat slanting, faintly resembling the Mongolian type. The mentality is never affected in the pure form of the condition.

The cases reported by Hutchison[6] are not typical of the class that we are considering, if one may judge by the photographs, and the apparent mental state of these children.

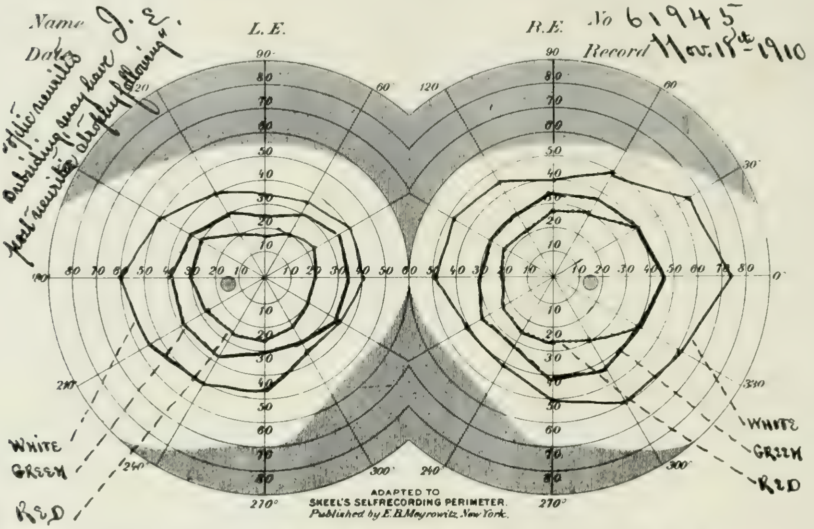

Fig. 8.—Perimetric charts showing changes in the color fields.

The most difficult problem to solve in this condition is presented by the eye changes. What causes the optic neuritis and the impediment to the return circulation through the ophthalmic vein? The latter condition may probably be accounted for by a certain degree of general increased intracranial tension, causing some stasis in the cerebral sinuses. There is no evidence to prove that the sphenoidal fissure is narrowed in these cases. There is, however, another factor of some importance in the production of the choked disk, as we shall see later. Let us attempt to answer the first part of the problem, the cause of the optic neuritis. The easiest solution was naturally the one that first suggested itself, and was consequently the one accepted by many of the earlier investigators, namely, a diminution in the caliber of the optic foramen caused by the change in the cranial form, this narrowing of the lumen producing neuritis by pressure. There can be no doubt that cases have been examined post mortem and narrowing of the foramen demonstrated, but it is equally certain that some instances have shown no apparent lessening in the foramen's size, and it has been proven by examination of a large number of crania of this type, from museums, that reduction in the size of the foramen was not even a common occurrence.

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[6] Hutchison: Proc. Roy. Soc. Med., Children's Section, 1910, 125.

It is difficult to understand why the optic foramen should become smaller because of any of the changes in the cranial form that we see in this condition. The foramen lies entirely in the sphenoid bone and is not cut across by any suture. Moreover, if these changes in the cranium were a cause of narrowing of any of the foramina, the optic would be among those least likely to be affected. There are other foramina, and especially fissures, that ought to present evidence of some such influence. It is more reasonable to suppose in those instances in which there has been a smaller optic foramen than normal, that the condition is the result, not the cause, of the changes in the optic nerve, the gradual adaptation of the opening to the atrophied nerve bundle. Much more important than the actual bony narrowing in any event would probably be the entrenchment on the lumen of the foramen by the thickened dural and pial sheaths of the nerve, and the exudate or infiltration in the intravaginal space (between dura and pia).

It is probable, however, that this thickening is simply contributory, and that the chief factor in the causation of the optic neuritis and secondary atrophy is the increased pressure to which the intracranial portions of the nerves are subjected by the long-continued increased tension of the intracranial contents, secondary in part to an increase of cerebrospinal fluid, in part to the pressure of the expanding brain.

This would also account for choked disk, which of course could not be due directly to any obstruction at the optic foramen. When it is remembered that the optic commissure and the beginning of the optic nerves lie directly in the orbital groove, with its hard, bony surface, and that increased intracranial pressure, especially if due to external hydrocephalic tension, must, for this reason, bear with especial intensity on this to a greater degree than perhaps on any other of the cranial nerves, it is not difficult to understand the occurrence of optic neuritis and atrophy in conditions associated with increase of intracranial pressure. Not only is the intracranial portion of the optic nerve exposed to this direct pressure, but also it has been conclusively proved, clinically and experimentally, that increased intracranial tension in the subdural space may be transmitted directly through the optic foramen into the sheath of the nerve itself, producing distention and inflammatory reaction with exudate in the orbital sheath of the nerve. Some of the choking of the disk may probably also be thus accounted for, by the interference of this exudate in the nerve sheath, with the venous backward flow through the first portion of the ophthalmic vein, which traverses the center of the optic nerve for a short distance after leaving the retina.

How extreme may be the necessity for the brain to adapt itself to very abnormal intracranial conditions is evidenced by a specimen of a bisected skull with its contents, from a case of acrocephalus, shown by Carpenter.[7] It indicated to what an extent the cerebrum is capable of adapting itself to the cranial form. It was so crumpled on itself that only a space of an inch separated the frontal lobe from the occipital, this space being occupied only by the pons and crura. The brain was otherwise well developed.

We cannot absolutely deny the possibility of the presence of a low grade chronic meningeal process in some of these cases, but nothing of the kind has ever really been proved, and the assumption rests merely on the hypothesis that a certain degree of pachymeningitis might produce premature ossification of the cranial vault by a stimulation of bone growth. We may answer this hypothesis, however, by asking why we do not have evidence of abnormal synostosis in all instances of pronounced pachymeningitis. I believe that the intercurrent appearance of headache, vomiting and convulsions, symptoms that have been ascribed to meningitis, are due to temporary rapid increase of intracranial tension, due to increase of the cerebrospinal fluid, or to transient circulatory disturbance. The appearance of these symptoms is quite common, and the headache may persist with considerable intensity for a long time. It will be noticed in my patient that the sudden appearance of headache and vomiting, coincident with a severe "cold," was the first thing that suggested to the mother that anything was wrong with the boy.

The defective vision is, however, often the first sign noticed, and it is usually noticed very early in infancy.

The condition which I have here described is, curiously enough, far and away more common in the male sex, and it is most interesting to note that premature ossification of the sutures is also much more commonly seen in males than in females.

What determines the precocious synostosis it is impossible to say.

591 Beacon Street.

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[7] Carpenter: Brit. Jour. Child. Dis., 1909, 273.

MUSCULAR HYPERTROPHY OF THE PYLORUS IN INFANCY*

HENRY LARNED KEITH SHAW, M.D., AND THOMAS ORDWAY, M.D.
ALBANY, N. Y.

This may be defined as an affection occurring in young infants characterized by forcible vomiting, constipation, visible peristalsis and frequently a palpable tumor at the situation of the pylorus produced by a marked increase in its muscle fibers. The disease has been described under the names "Hypertrophic Pyloric Stenosis in Infants," "Congenital Spastic Stenosis," "Congenital Pyloric Stenosis," and "Spastic Hypertrophic Pyloric Contracture."

Osler discovered a typical description of this disease written by Dr. Hezekiah Beardsley in a volume entitled "Cases and Observations by the Medical Society of New Haven County in the State of Connecticut," published in New Haven in 1787. It will not be out of place to quote liberally from this paper which is remarkable for the accuracy of observation and quaintness of diction.

> "A child of Mr. Joel Grannis, a respectful farmer in the town of Southington, in the first week of its infancy, was attacked with a puking, or ejection of the milk, and of every other substance it received into its stomach almost instantaneously, and very little changed. The feces were in small quantity and of an ash color, which continued with little variation till its death. For these complaints a physician was consulted, who treated it as a common case arising from acidity in the prima via; the testaceous powders and other absorbents and correctors of acid acrimony were used for a long time without any apparent benefit. * * * I was at first inclined to attribute the disorder to a deficiency of bile and gastric juices, so necessary to digestion and chylification, joined with a morbid relaxation of the stomach, the action of which seemed wholly owing to the weight and pressure of its contents, as aliment taken in small quantities would often remain on it, till, by the addition of fresh quantities, the whole, or nearly all, was ejected; but his thirst, or some other cause, most commonly occasioned his swallowing such large draughts as to cause an immediate ejection, and often-times before the cup was taken from his mouth. * * * A number of the most respectable medical characters were consulted and a variety of medicines were used to little or no effect. His death, though long expected, was sudden, which I did not learn till the second day after it took place. This late period, the almost intolerable stench, and the impatience of the people who had collected for the funeral prevented so thorough an examination of the body, as might otherwise have been made. * * * I next examined the stomach, which was unusually large, the coats were about the thickness of a hog's bladder when fresh and distended with air; it contained about a wine pint of fluid exactly resembling that found in the vesicles before mentioned, and which I supposed to have been received just before his death. The pylorus was invested with a

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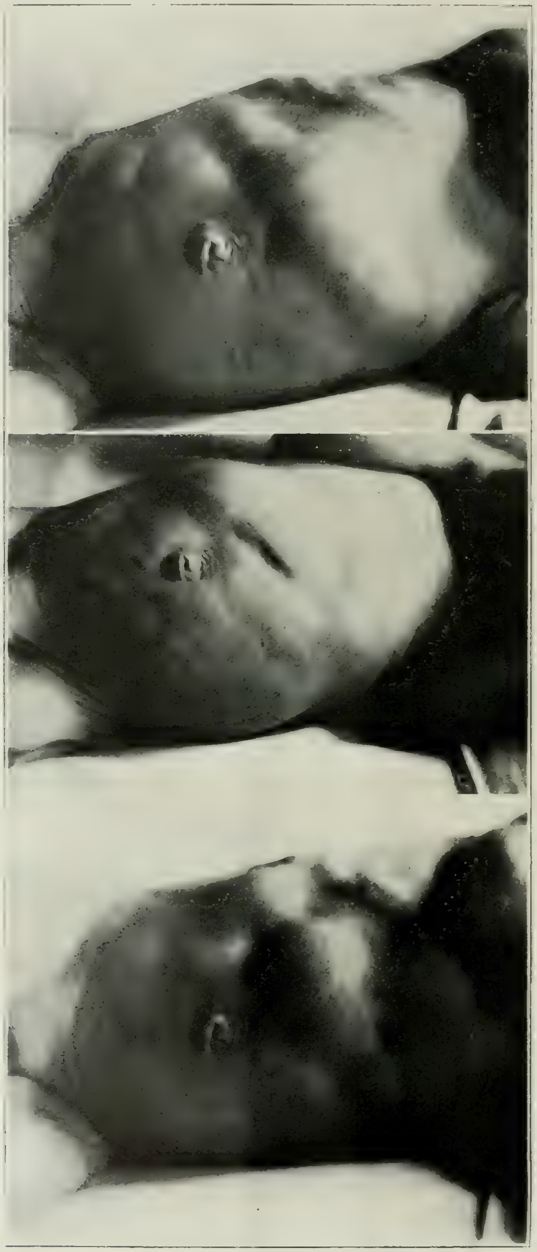
*Read at the meeting of the American Pediatric Society, Lake Mohonk, May 31, 1911.



Figs. 1, 2 and 3.—Visible peristalsis of the stomach. Case 3.

> hard compact substance, or schirrosity, which so completely obstructed the passage into the duodenum, as to admit with the greatest difficulty the finest fluid; whether this was the original disorder, or only a consequence, may perhaps be a question. In justice to myself I ought to mention that I had pronounced a schirrosity in that part before the child's death."

Williamson published an account of this condition in a 5-weeks-old infant with the autopsy findings in the London and Edinburgh *Journal of Medicine* in 1841.

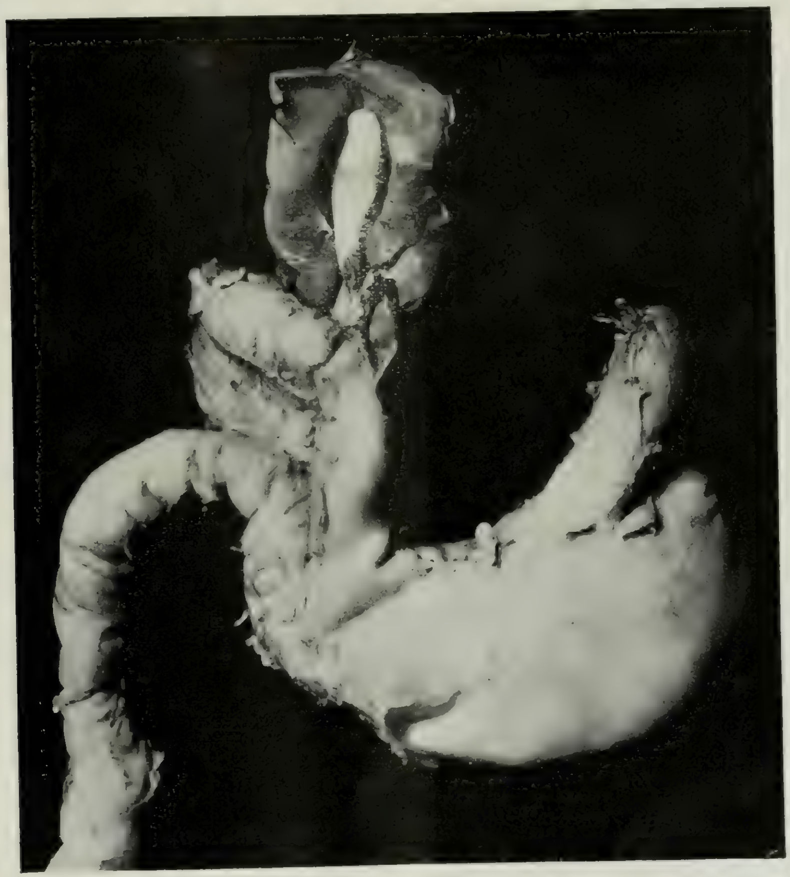


Fig. 4.—Case 4. Stomach, duodenum, fragment of liver and gall-bladder: the upper part of the small intestine is sutured to the stomach just below the pylorus (natural size).

No further mention of this disease in infants appeared in the literature until Hirschsprung, a Danish physician, reported two cases before the German Pediatric Society in 1887. He found that the pylorus was thickened and that the muscle fibers were increased. Pfaundler called attention to the fact that two distinct groups of cases had been classified under one head. He showed that there was both a functional and organic closure of the pylorus and his views are now almost universally accepted. A careful examination of the literature by one of us (Shaw) in 1904 revealed 117 cases while Ibrahim collected over 400 cases in 1908 and a number of cases have been reported since then. This condition is therefore by no means uncommon and must frequently be overlooked.

Pfaundler found that the first vomiting or onset of the disease was between the fourth and fourteenth days in 50 per cent. of the cases, from the second to third week in 25 per cent., and from the third to sixth week in 25 per cent. Five out of nine of our cases started in the first and second weeks of life, two in the third week, one in the fourth and one after the fourth.

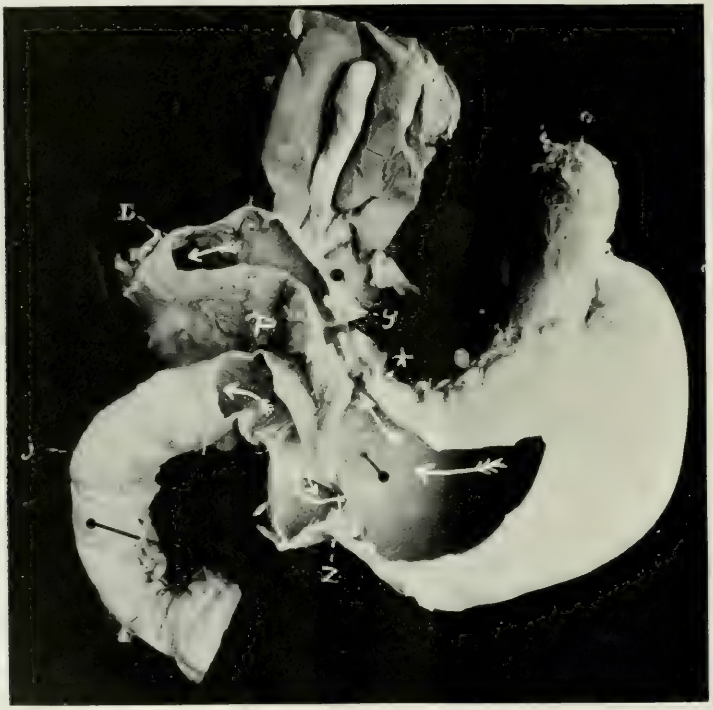


Fig. 5.—Case 4. Same as Fig. 4. A portion of the anterior walls of the stomach, duodenum and jejunum have been removed showing the stenosed pylorus with greatly thickened walls (x-y). Here, as indicated, fragments have been removed for sectioning longitudinally (Figs. 6, 7, and 8) and transversely (Figs. 9 and 10). The natural and artificial food channels are indicated by arrows. z, large, patent gastro-enterostomy opening; j, jejunum; d, duodenum; p, pancreas; o, esophagus (natural size).

Boy babies are affected, according to Ibrahim, about four times as frequently as girls, but in our cases five of the nine were boys. Five of our nine were first-born babies and in two families subsequent children have shown no gastric disturbances. In one family the first child is strong and healthy, the second child died after an operation to relieve the stenosis (Case 3) and the third child died when 6 weeks old from a typical attack of this disease. This is the only instance among our cases in which there appeared to be any family tendency.

Nearly all the cases of pyloric stenosis occur in breast-fed infants, which is contrary to nearly all the affections of the digestive tract.

SYMPTOMS

A healthy and robust child in the first weeks of life is suddenly seized with violent *vomiting* without apparent cause. At first this occurs irregularly but later increases in frequency, often after each feeding. Examination of the breast milk shows it to be normal. Modifications of cow's milk, changes in quantity or quality of the food or of the intervals of feeding have no effect on the vomiting. It is forceful and projectile and occurs suddenly without warning. It is variable in amount, and the quantity of fluid thrown up is surprising. The child will apparently retain several of its feedings but suddenly will throw up all the previous feedings. Six ounces may be thrown up in a jet-like explosion. The vomited matter consists of slightly digested milk mixed with mucus. It never contains bile.

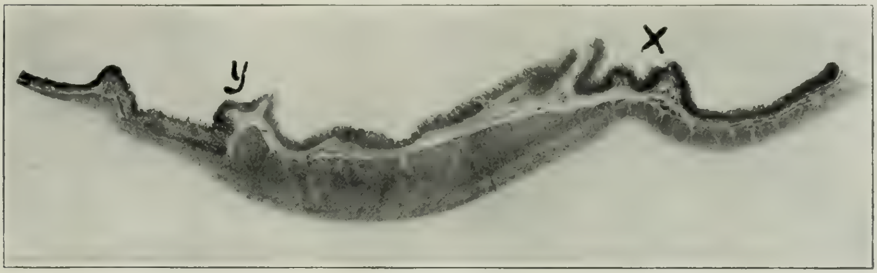


Fig. 6.—Case 4. Longitudinal section of wall of pyloric canal showing the greatly thickened muscular wall. The duodenal end of the "canal" is indicated by "y" and the gastric end by "x". These points are well marked, the former by the duodenal submucous or Brunner's glands, and the latter by a definite indentation; here the thickening of the muscle coat begins. Hematoxylin-eosin stain. (Mag. x 4.)

This vomiting is not controlled by the usual medicinal remedies. Lavage may reduce the vomiting to once or twice a day. The tongue remains clear and the breath sweet.

Constipation and impaired nutrition are directly dependent on the vomiting. The constipation is really deficient defecation resulting from the diminished intake of food and fluid. Cases have been observed in which no bowel movement could be obtained for twelve days. The stools are small in amount, dark green, very offensive, and contain much mucus. The urine is scanty and high colored.

The *weight* of the infant is the index of his nutrition. The loss in weight in this disease can amount to 1 ounce or more a day. There is a progressive emaciation which is shown later by extreme exhaustion, subnormal temperature, depressed fontanel, sunken cheeks, etc.

The lower part of the *abdomen is flat* and even sunken in, while the upper part is distended and prominent. This gives the abdomen a characteristic appearance.

The most characteristic symptom and one that is pathognomonic of this condition is the *visible peristaltic contraction* of the stomach. This has been termed "stomach stiffening" and is due to the strong muscular contraction of the narrow pylorus. The stomach appears to stand up on itself. This is seen during sleep as well as when the child is awake. The wave starts from the left side and is about the size of a hen's egg. The protruding part is often surrounded by deep retraction in the abdominal wall. Before it disappears to the right another wave appears where the first started. Hour-glass contractions may occur owing to the two waves running close behind each other. This visible peristalsis apparently is not painful, which is not the case with spastic contraction of the pylorus with which it is often associated.

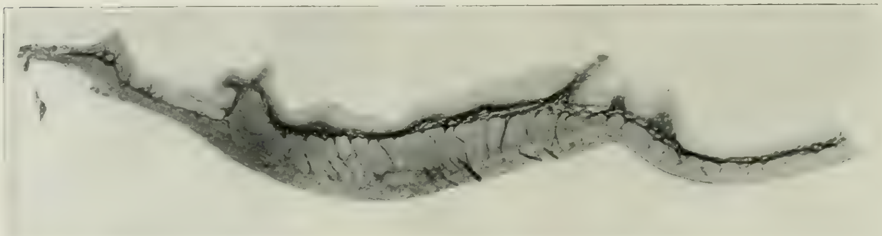


Fig. 7.—Case 4. Section same as Fig. 6, stained by Van Giesen's connective tissue stain. The large amount of muscle tissue is in marked contrast to the connective tissue which appears black. (Mag. x 4.)

An equally characteristic and pathognomonic symptom is a *palpable enlargement of the pylorus.* This is not regularly present especially in early cases. The pylorus was markedly enlarged in all of our six patients operated on, and in none of them could the pylorus be palpated through the abdominal wall.

Dilatation of the stomach is present in advanced cases depending on the degree and duration of obstruction but is absent in the early stages, as the food is ejected as soon as the stomach is overdistended. The stomach contents may be retained over several feedings and then ejected, showing that little or no food passes out of the stomach.

Several authors emphasize the presence of *hyperacidity*. The increased acidity may be due to hyperchlorhydria or an increase in fatty acids.

PATIENTS OPERATED ON

Case 1.—E. S., first child, breast-fed from birth. Vomiting commenced about the third month; admitted to St. Margaret's December, 1902, aged 6 months; weight 15 pounds 8 ounces; uncontrollable vomiting, visible peristalsis, constipation. The symptoms continued despite treatment and there was a steady loss in weight. Operation (anterior gastro-enterostomy) at the Child's Hospital by Dr. Elting in June, 1903. Weight 12 pounds 1 ounce; "Stomach greatly dilated, pylorus firm and thickened, lumen greatly reduced and stenosis pronounced." No bile was ever detected in the vomitus before operation but was present afterwards.

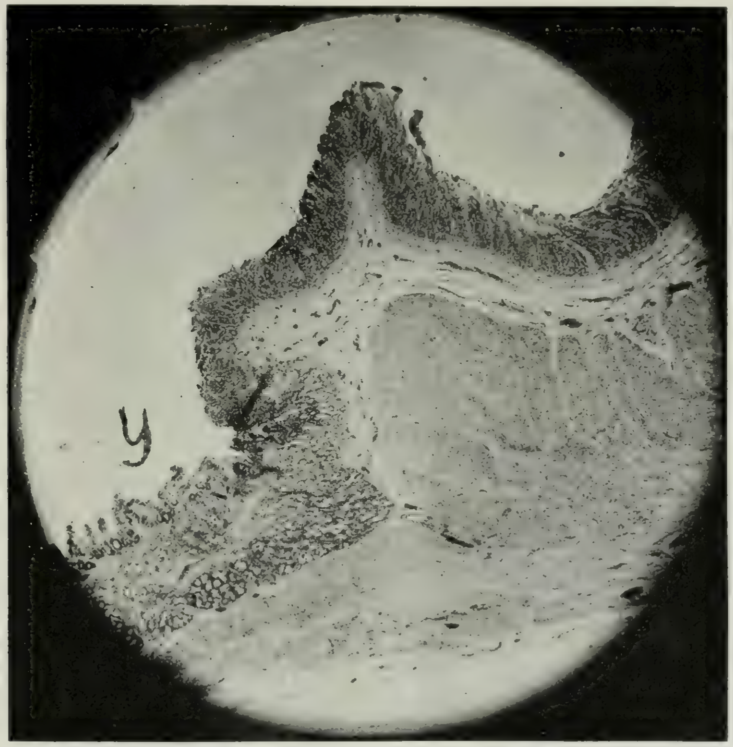


Fig. 8.—Case 4. Portion of Fig. 6 showing duodenal end of wall of pyloric canal. The submucous (or Brunner's) glands begin at "y," to the left is duodenum and to the right the pylorus. The thickness of the walls is in marked contrast. Minute black foci scattered through the submucosa, muscularis, and serosa indicate the inflammatory changes above referred to. (Mag. x 40.)

The child made a good recovery and gained 9 pounds in five months, and is now a large, well-nourished girl without any stomach trouble.

Case 2.—E. B. (referred by Dr. Pearson of Schenectady); first child; breast-fed. Vomiting commenced at the end of the first week and was projectile in character; visible peristalsis and constipation.

Operation (posterior gastro-enterostomy) by Dr. Elting, Nov. 23, 1906, when the child was three weeks old. Died Nov. 28, 1906. No post-mortem allowed. Operation protocol reads as follows:

"On opening the abdominal cavity, a large distended stomach ballooned out. The intestines were collapsed and appeared as mere ribbons. There was complete stenosis of the pylorus due to a tumor the size of a small pigeon's egg and regular in outline. It was impossible to force gas through at this point. After anastomosis the intestines began to dilate and fill with gas."

Case 3.—M. M., referred by Dr. Maby of Mechanicsville; second child; first child was strong and healthy. This child was breast-fed and commenced vomiting at three weeks. It was admitted to St. Margaret's Nov. 1, 1909. There was visible peristalsis (Figs. 1, 2, 3). Vomiting was controlled by lavage, but the stomach retained all food. There was constipation. Weight at birth 7 pounds; at five weeks 5 pounds 14 ounces.

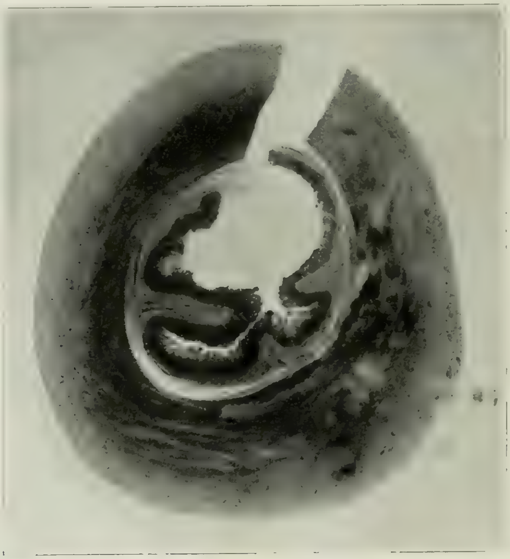


Fig. 9.—Case 4. Transverse section of walls of pyloric canal showing the greatly thickened muscular coat. Hematoxylin and eosin stain. (Mag. x 6.)

Operation (posterior gastro-enterostomy) by Dr. MacDonald, Nov. 4, 1909. Weight at that time 5 pounds 9 ounces. Child died Nov. 5, 1909; no post-mortem allowed. At the operation a firm tumor was found at the pylorus. The stomach was distended and the intestines collapsed.

A third child was born last September. Two weeks later it began to vomit. There was visible peristalsis and Dr. Maby wrote that it was a typical case of hypertrophic pyloric stenosis. On account of their experience with the other child they would not permit an operation, and the child died in October when 6 weeks old.

Case 4.—C. D.; referred by Dr. Kurth, Schenectady; first child was breast-fed; began vomiting at two weeks; admitted to St. Margaret's Jan. 8, 1910, when five weeks old; weight 7 pounds, 8 ounces. There was visible peristalsis and constipation.

Operation (posterior gastro-enterostomy) by Dr. Elting, Jan. 8, 1910. Weight 7 pounds 1 ounce: "Markedly dilated stomach with a definite hard and firm construction at the pylorus. There is comparatively complete obstruction." The child made a good recovery and was discharged Feb. 6, weighing 8 pounds, 9 ounces. Returned to hospital Feb. 24, with severe ileo-colitis. There was no vomiting. Died of exhaustion Feb. 28, aged two months, three weeks. Autopsy by Dr. Ordway (Figs. 4, 5, 6, 7, 8, 9, 10).

Case 5.—T. K., referred by Dr. Shaw of Lansingburg. First child and breast-fed. Vomiting commenced on the tenth day. There was visible peristalsis and constipation. The child was admitted to St. Margaret's March 15, 1911, and weighed 7 pounds, 3 ounces, at three weeks. Weight at birth was 8½ pounds.

Operation (posterior gastro-enterostomy) by Dr. Elting, March 19. Weight 6 pounds, 12 ounces. Died March 21. No post-mortem allowed. At operation there was dilated stomach, collapsed intestines, and a large pyloric tumor.

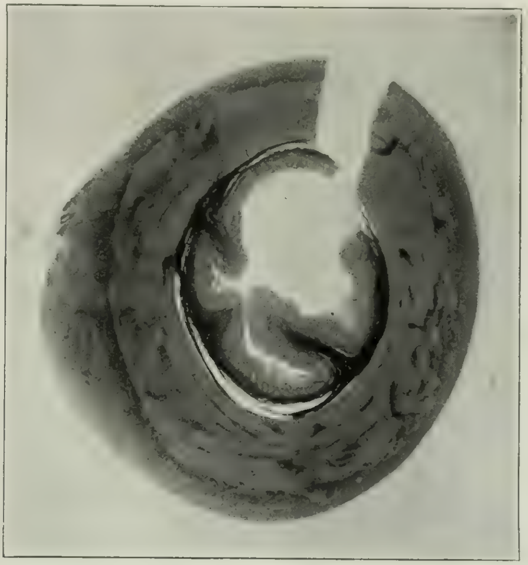


Fig. 10.—Case 4. Section same as Fig. 9 stained by Van Giesen's connective tissue stain. The large amount of muscle tissue is in marked contrast to the connective tissue which appears black. (Mag. x 6.)

Case 6.—M. C., referred by Dr. Lamont of Catskill; second child; first was strong and healthy; child was breast-fed and began vomiting at two weeks. Weight at birth was said to be 8 pounds; child was weaned at three weeks and all methods of feeding were employed. There were visible peristalsis, constipation and vomiting. The emaciation was extreme.

Admitted to St. Margaret's April 17, 1911, at 8 weeks and weighed 5 pounds, 11 ounces. The vomiting was controlled by lavage but the entire previous feedings would be removed at the next lavage. The child lost 8 ounces in four days.

Operation (posterior gastro-enterostomy) April 21, by Dr. Elting. The operation showed dilated stomach, collapsed intestines and very large pylorus. The stomach was removed and sections prepared by Dr. Ordway (Figs. 11, 12, 13, 14, 15, 16, 17).

Case 7.—H. P., first child, was breast-fed for first three weeks. Vomiting commenced at second week. Weight at birth 7½ pounds. Admitted to St. Margaret's Aug. 21, 1906, when 6 weeks old and weighed 6 pounds, 14 ounces.

There were visible peristalsis and constipation. The peristalsis was visible for several months and there was a palpable pylorus. Weight September 2, 6 pounds, 7 ounces. The child improved slowly. Lavage was given twice a day and the child was nourished by rectal nutrient enemata. Weight at discharge December 20, 1906, 9 pounds, 5 ounces. He is now a strong, healthy boy.

Case 8.—R. C. was the second child and weighed at birth 7¾ pounds. He was breast-fed at first and later had a wet-nurse. Vomiting came on suddenly at four weeks. There were visible peristalsis and constipation. Lavage was employed by the mother. The weight at six weeks was 6 pounds. The condition lasted five months, and the child is now apparently healthy and strong.

Case 9.—E. G. was the second child. The first was strong and healthy. Breast-fed for eight months. Mixed feeding was begun at five months. Weight at birth was 8 pounds. Lowest weight was 5 pounds, 8 ounces.

Vomiting commenced at the third week. There were visible peristalsis and marked constipation. A pyloric tumor was very plainly felt. Weight at 9 months was 8 pounds, 11 ounces. The mother used lavage twice a day for several months.

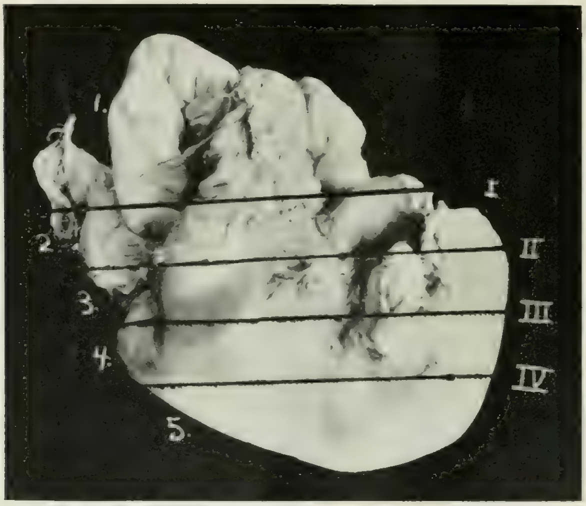


Fig. 11.—Case 6. Stomach, duodenum, and adjacent portion of small intestine of infant. The jejunum is sutured to the posterior wall of the stomach near the pylorus. I-IV indicate the location, and the plane of the sections which divide the specimen into five fragments (1-5) see Figs. 12 and 17 (5/7 natural size).

PATHOLOGY

Introduction

Secretion and digestion are often regarded as the most important functions of the stomach; absorption and assimilation, it is agreed, are chiefly performed elsewhere. We are apt to overlook the functions of storage and motility. The importance of these is emphasized in many animals; in the rat, for example, a large part of the stomach is lined by stratified squamous epithelium with a distinct horny layer, the secretory glands being situated in the small pyloric portion. The muscle coats are more evident at the pylorus. The circular muscles are usually distinct and reach their maximum thickness just before the beginning of the duodenum. The oblique fibers are not so well defined and may merge into the circular or the longitudinal muscles.

Discussion of Pathological Findings

In these cases most writers describe a tumor occupying the position of the distal part of the pylorus. We shall designate this as the "pyloric canal," which connects the smaller funnel-shaped, or pyloric, portion of the stomach with the duodenum. The proximal end is indicated by a constriction (Fig. 6 x) and the distal by the duodenal submucous glands.

The tumor-like enlargement varies from 1.5 cm. to 3 cm. in length and 0.75 to 1.5 cm. in thickness. It is described by Scudder as a resilient cylinder about the size of a hickory nut. Its consistency is very firm, so that Dilz speaks of it as a cartilaginous tube. The tumor is composed of the greatly thickened muscle coat of the "pyloric canal," chiefly of the inner or circular layer of fibers. Our measurements[1] in general agree with those of other observers. No difference was found in the length of the nuclei in the normal control case and in the two cases of hypertrophy of the pylorus, although the thickness in the latter two was somewhat less. The caliber and patency of the lumen of the "pyloric canal" is variable and the measurements depend in part on the method by which

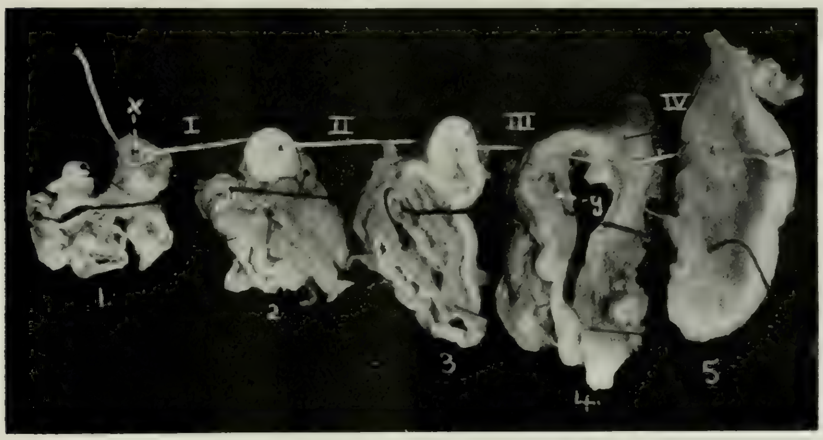


Fig. 12.—Case 6. Five sections showing four serial surfaces 1-I, 2-II, 3-III, 4-IV (see also Fig. 17). A white cord passes through the natural food channel, the walls of which at the pyloric portion of the stomach are greatly thickened (sections 2 and 3); the duodenum is of normal thickness (section I-"X"). A dark cord passes through the gastro-enterostomy opening (section 4-"y"), and indicates the course of the artificial food channel (½ natural size).

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[1] See table of measurements.

the specimen is preserved. In Case 4 a tapering probe was gently inserted through the "canal" and where the least resistance was encountered, the circumference of the probe was found to be 1.3 cm. By a similar method Wolbach in one case found a lumen of 2 cm. in circumference. The canal in Case 4 was carefully packed with absorbent cotton and after hardening in 10 per cent. solution of liquor formaldehydi (formalin) the diameter of the lumen was 2 x 3 mm. In Case 6, on the other hand, the specimen had been preserved in toto in 10 per cent. solution of liquor formaldehydi and the diameter of the lumen, which was practically obliterated by folds of mucosa, was 0.14 x 0.49 mm. A normal control hardened by slowly injecting through it and then immersing in 10 per cent. solution of liquor formaldehydi measured 4.0 x 4.9 mm. in diameter.

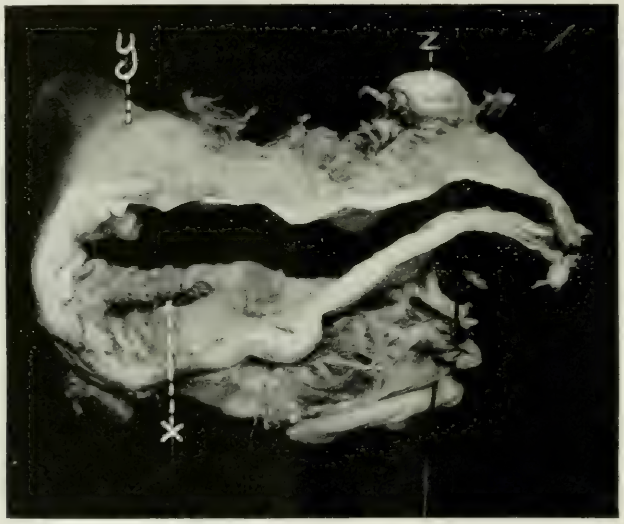

Fig. 13.—Case 6, Section 4, surface 4-IV, showing large patent gastro-enterostomy opening at "x"; the outer surface of a portion of the pyloric thickening is seen at "y"; "z" indicates the esophageal opening (natural size).

The test of functional patency by hydrostatic pressure is fallacious, for the redundant folds of mucous membrane may act as valves; these and the subsequent shrinkage due to the preserving fluid may give a false appearance of almost absolute impermeability to the pyloric canal. There is little doubt, however, that the lumen is encroached on by the ridges or folds of mucosa projecting into it. In some cases the mucous membrane is hypertrophied.[2] Dilated, cystic and flattened glands with excess of mucus were noted by Wolbach. Our cases showed an occasional dilated gland, but not more marked than in control cases. Longitudinal folds or ridges project into the lumen of the pyloric canal. Case 4 showed three marked folds and Case 6, four; in the control there were two. Dilz describes three ridges of mucosa projecting into and completely occluding the lumen. Cervix-like projections of the mucosa similar to those bulging toward the duodenum may also be found at the proximal end of the pyloric canal. They occur, though less marked, in normal cases. It is these folds and ridges which form the so-called "pyloric valve."

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[2] See measurements, Cases 4 and 5, table of measurements.

Various inflammatory changes of the pylorus have been described in these cases. Larkin believes there is an increase in connective tissue.

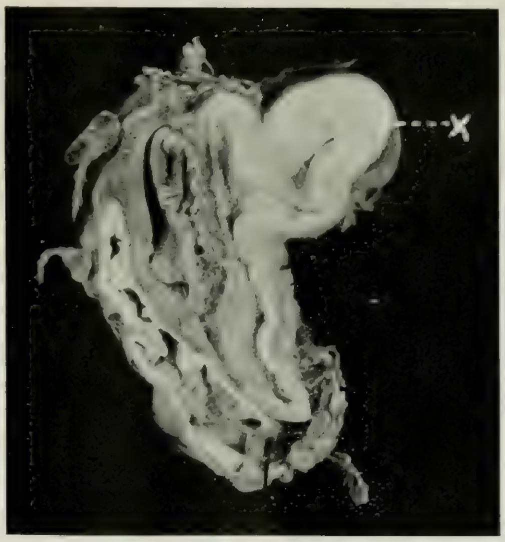

Fig. 14.—Case 6, Section 3, surface 3-III, showing great thickening of the pyloric walls in the vicinity of "x". The walls of the cardiac portion of the stomach are of normal thickness (natural size).

Weill and Pelm consider the hyperplasia of the pyloric muscles secondary to an inflammatory process, while Fredet and Guillinot think that an inflammatory swelling of the mucosa and spasm merely aggravate the stenosis.

In our cases, one, Case 4, showed, microscopically, moderate chronic and slight acute inflammatory changes in the mucous, muscle and serous coats; in Cases 6 and "X" (control) there was no evidence of inflammation of the walls of the pyloric canal. The stomach, in cases of pyloric stenosis in infants, has been described as larger than normal by some writers and others have found it smaller; its wall also in some cases is thinned and in others increased in thickness. In Case 4 the muscles of the stomach wall near the pyloric canal were 0.7 mm and in the control 0.9 mm. in thickness.

The duodenum, when mentioned, has been regarded as normal. In our own cases the thickness of the muscle coat was 0.49 mm. in Cases 4 and 6 and in that of the control "X." 0.16 mm.; this, however, may be within normal limits.

AUTOPSY AND LABORATORY FINDINGS

Case 4.—Post-mortem examination, Bender Laboratory A-10-17, by Dr. Ordway, for Dr. Shaw, at St. Margaret's House, Feb. 28, 1910, at 9:30 a. m.

C. D., aged 2 months and 3 weeks, 7 hours post-mortem.

Body is that of a fairly well developed, poorly nourished, emaciated male infant. Bony framework is everywhere prominent. Skin hangs in folds. Eyes are sunken. External orifices are negative. There is very slight lividity of dependent portions and no *rigor mortis*. The abdomen is prominent, slightly elevated above the level of the chest. In the median line between the ensiform and umbilicus there is a whitened linear scar 7 cm. in length. There is no edema. The axillary and inguinal glands are slightly enlarged, distinctly palpable; otherwise the superficial glands are negative.

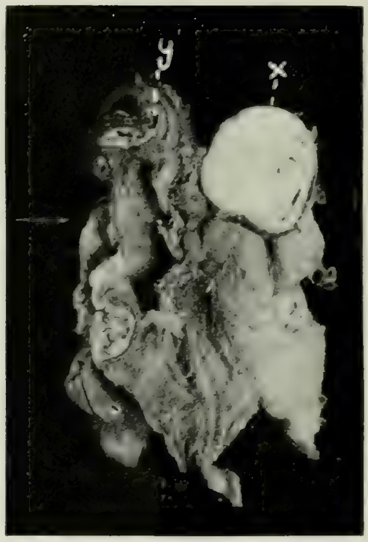

Fig. 15.—Case 6, Section 2, surface 2-II, showing great thickening of the pyloric walls at "x". The jejunum is seen at "y" (natural size).

Note.—Autopsy incision restricted to surgical incision above mentioned.

Peritoneal Cavity.—The right lobe of the liver, anteriorly, in the median line and the omental tissue are adherent to the inner aspect of the operative wound above described; otherwise the peritoneal cavity is normally smooth, moist, and glistening. The pleural and pericardial cavities, the heart, lungs, spleen, liver, pancreas, adrenals, kidneys, aorta and genital organs are normal.

Gastro-Intestinal Tract.—The upper portion of the cardiac end of the stomach to the left of the esophagus is adherent to the adjacent peritoneum of the diaphragm by delicate fibrous adhesions. The stomach is small, does not reach the umbilicus and is empty. Rugæ are prominent. The walls of the pylorus are greatly thickened for a distance of 2 cm., having the consistency of a firm. hyperplastic gland and forming a distinct ovoid tumor-mass in the region of the pylorus. This is in marked contrast to the walls of the duodenum, which are thin and collapsed, and to the walls of the cardiac portion of the stomach, which are of normal thickness. A tapering probe is inserted through this thickened portion of the pylorus without difficulty until a point 1.3 cm. in circumference is reached; that is, the circumference of the pyloric opening after death, with practically no pressure, is 1.3 cm. On the posterior wall of the stomach 1.5 cm. below the pyloric opening, which is marked by protruding folds of mucous membrane, is a large opening into the jejunum; the latter is firmly adherent to the posterior wall of the stomach (Figs. 4 and 5. The diameter of this opening is 1.4 cm. Pressure on the gall-bladder causes yellowish fluid to exude into the duodenum from the ampulla. The small and large intestines contain a small amount of bright yellow, semi-solid material with numerous light yellowish shreds. Peyer's patches and solitary follicles are prominent. The intestines are markedly distended by gas.

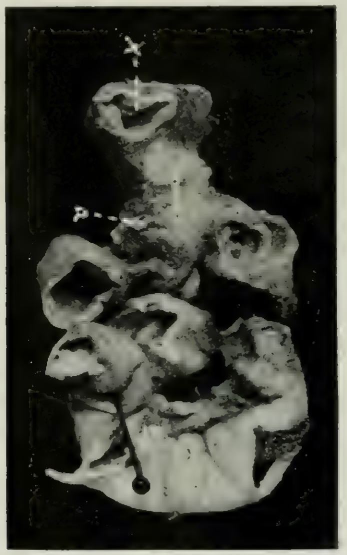

Fig. 16.—Case 6, Section 1, surface 1-I, showing duodenum "x"; adjacent to the pylorus is the pancreas "p"; the other openings represent sections of the duodenum and coils of jejunum (natural size).

Anatomic Diagnoses.—Emaciation, hypertrophy of pylorus, gastro-enterostomy; healed incised wound of abdominal wall, adhesions of omentum and liver to abdominal wall.

Microscopic Examination.—The stomach, duodenum and adherent jejunum are carefully filled with cotton saturated with 10 per cent. solution of liquor formaldehydi and these organs hardened in as nearly normal shape as possible. Particular care is taken that the stenosed pyloric and the artificial gastroenterostomy openings may be prevented from distortion by shrinkage (Figs. 4 and 5). Fragments removed from the wall of the "pyloric canal," as indicated in Figure 5, were cut in longitudinal and transverse sections and stained by hematoxylin and eosin and Van Giesen's connective tissue stains (Figs. 6 to 10). The great thickening of the wall is due to an increase in muscle tissue and chiefly to the circular fibers. There is slight atrophy of the glands in the mucosa and an increase in the interglandular tissue. An occasional gland is distended by lymphocytes and polymorphonuclear leukocytes. Scattered through the submucosa, muscularis and serosa, are numerous foci of lymphoid cells and few polymorphonuclear leukocytes; in many places similar cells distend the perivascular lymphatics. There is no increase in connective tissue. In the serosa there is a small amount of old yellowish pigment.[3]

Case 6.—Michael C. Bender Laboratory, A-11-42. Post-mortem examination performed by Dr. Donhauser and restricted to surgical incision and examination of stomach, duodenum and jejunum.

Stomach, duodenum and portion of adjacent small intestine of an infant. The specimen was received in toto in 10 per cent. solution of liquor formaldehydi. It is somewhat shriveled by the preserving fluid and measures 7x5 cm. In the region of the pylorus is a hard tumor mass measuring 2x1.5 cm. The jejunum is sutured to the stomach on the posterior aspect near the pylorus (Fig. 11). Serial sections as indicated, I, II, III, IV, are made and divide the specimen into five fragments 1, 2, 3, 4, 5 (Fig. 12). A white cord passes through the natural food channel, the walls of which at the pyloric portion of the stomach are greatly thickened (Figs. 12, 14, 15, 17), sections 3 and 2. The wall of the duodenum is of normal thickness (Fig. 12, Section 1 "X", and Fig. 16).

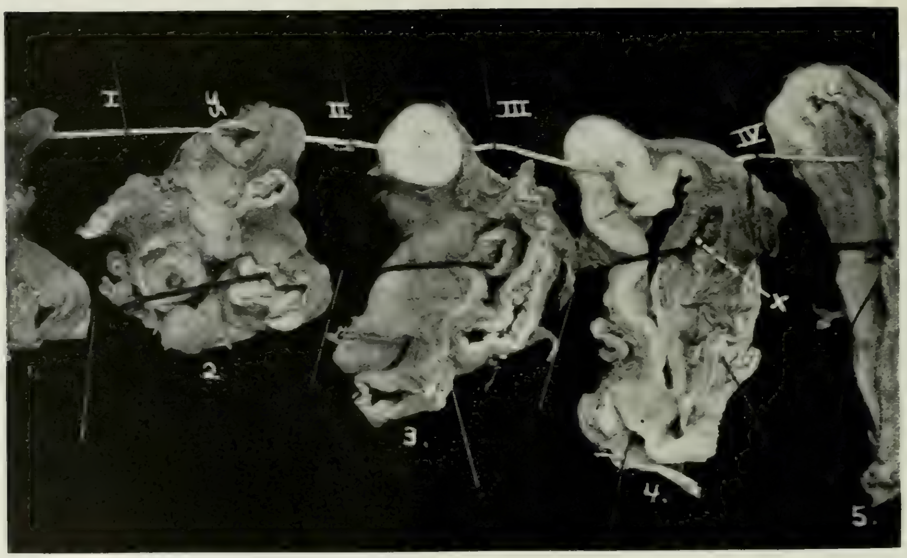

Fig. 17.—Case 6. Three sections and portions of two others showing three serial surfaces, 2-I, 3-II, 4-III. White cord passes through the natural food channel, the walls of which at the pyloric portion of the stomach are greatly thickened (3 and 4); the duodenum is of normal thickness (2 "y"). A dark cord passes through the gastro-enterostomy opening (4 "x") and indicates the course of the artificial food channel (5/7 natural size).

Note.—The surfaces here seen are the reverse of those shown in Figures 12 *et seq.*

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[3] These inflammatory changes may have been secondary to the healing of the gastro-enterostomy wound. Patient 6 died before such change could have occurred.

A dark cord passes through the gastro-enterostomy opening and indicates the course of the artificial food channel (Figs. 12 and 17). The thickening of the pylorus is not abrupt on the stomach side, but involves almost the entire pyloric portion of the stomach and gradually increases in thickness as the duodenum is approached. At the junction of the duodenum, where the submucous (Brunner's) glands begin, this thickening is at a maximum and here ends abruptly. The gastro-enterostomy opening is large and the canal is patent. The intestine and stomach are firmly approximated and there is no leakage or suppuration.

Microscopic Examination.—Fragments removed from the thickened wall of the pyloric canal, cut in transverse and longitudinal section, and stained by hematoxylin and eosin, show no pathologic change other than the great increase in the thickness of the muscle coat, chiefly of the circular fibers. These fibers appear normal.[4]

CASE "X" (Control).—Post-mortem examination by Dr. Kellert. Bender Laboratory A-11-47. May 25, 1911. Name unknown. Female infant, 8 months old. Child died with cerebral symptoms. Examination restricted to chest and abdomen, all the organs of which appeared normal. Stomach and duodenum hardened by carefully injecting and then immersing in 10 per cent. solution of liquor formaldehydi. Fragments were removed from the wall of the apparently normal pyloric canal, sectioned transversely (Fig. 18) and longitudinally (Fig. 19,[5] and stained by hematoxylin and eosin. Microscopic examination reveals no pathologic changes. Although this child was 8 months old, it was taken as a control to Cases 4 and 6, which were, respectively, 11 weeks and 8 weeks; notwithstanding this great difference in the age, the walls of this normal pyloric canal, as shown in Figures 18 and 19, and as indicated in the table of measurements, are in striking contrast to those of the pyloric canals in the cases (4 and 6) of muscular hypertrophy of the pylorus.

TABLE OF MEASUREMENTS, CASES 4, 6, AND "X" (CONTROL)

	Case 4 ..... mm.	Case 6 ..... mm.	Case "X" (Control) mm.
Length of pyloric tumor "pyloric canal"	16	18	11
Thickness of tumor, external diameter	12	14	9
Thickness of muscle layers	2 to 3	3 to 3.5	1 to 1.6
Thickness of circular fibers	1.64	2.57	0.98
Thickness of oblique and longitudinal fibers....	0.56	0.45	0.16
Diameter of lumen	3.0 x 2.0	0.49x0.14	4.9x4.0
Width of serosa	0.16	0.13	0.08
Thickness of mucosa and submucosa, from top of folds	1.8 to 3.5	3.5	2.0
Thickness of mucosa and submucosa, base of folds	1.06	1.1	0.82
Thickness of epithelium	0.41	0.90	0.49
*Mucosa, number of folds.....................	3	4+	2+
Stomach, thickness of muscle coats near "pyloric canal"	0.7	—	0.9
Duodenum, thickness of muscle coats near pylorus	0.49	0.49	0.16
Muscle nuclei, width	1.9 to 2.5	2.0 to 2.5	3.8
Muscle nuclei, length	28 to 34	28 to 34	28 to 34

*When small irregularities are present as well as the distinct folds, they are indicated by + following the number of folds designated.

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[4] See also table of measurements.

[5] Owing to a mistake in reproducing, Figures 6 and 7 were reduced from mag. x 6 to mag. x 4, while the "control," Fig. 19, was reduced from mag. x 6 to mag. x 5½. Because of this the contrast is not evident in these longitudinal sections, but is shown well when Figs. 9 and 10 are compared with Fig. 18.

PATHOGENESIS

There are a number of theories and conjectures concerning the pathogenesis of this condition. The earlier writers considered it a congenital organic defect due to excess of development. Cautley claimed that this was a primary hypertrophy, an instance in which "Nature in her extreme anxiety to provide an efficient pyloric sphincter, has over-exerted herself, and produced too great an amount of muscular tissue."

Flynn considered it an atavistic deformity analogous to the gastric mill in insects and crustacea and the gizzard in birds, or a reversion to the edentate pylorus seen in the armadillo. The assumption that there was a true tumor has not been proved histologically.

The term "congenital" is misleading as no true hypertrophy has been found in fetal life or at birth. The symptoms rarely if ever appear before the end of the first week, which is irreconcilable with the hypothesis of a congenital obstacle.

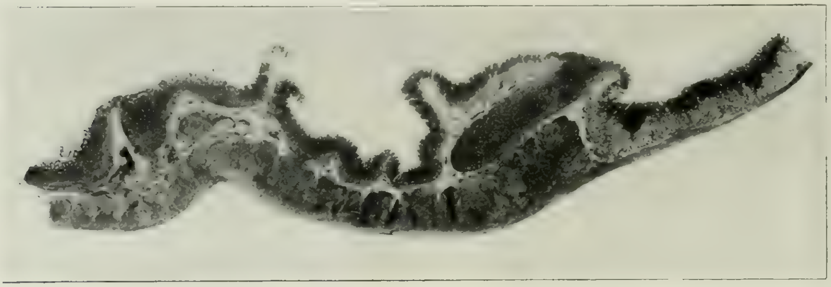

Fig. 18.—Case "X" (Control).—Longitudinal section of wall of normal pyloric canal. Compare with Fig. 6 (Mag. x 5½).

The later writers, as a result of the study of a large number of cases, are almost unanimous in the opinion that the hypertrophy or muscular hyperplasia is a secondary manifestation. This is the result of a spasm or incoordination of the gastric muscles. The spasm may start as a reflex spasm of the gastric mucosa incited by erosions, fissures, over-activity, hyperacidity, too high fat in the food, increased nervous irritability, etc.

Still has advanced an ingenious theory that the spasm is a kind of "stomach stuttering" in which the muscular action of both ends of the stomach is antagonistic. This he claims is analogous to the disturbance of coordination which is evident in hiccough or in the stuttering which is almost physiologic in the young child who is learning to talk.

Case 1 of our series shows conclusively that spasm of the pylorus will produce a marked hypertrophy.

COURSE

The course is slowly progressive and the condition may last from three to twenty months. The duration depends on the degree of stenosis. In cases in which recovery occurs the vomiting gradually subsides, constipation improves and the baby begins to gain in weight. This disease must be considered a very grave affection. Dr. John Thomson's statistics show that four children recovered out of seventeen treated medically, or a mortality of about 76 per cent., while eight recovered out of twenty-three treated surgically, or a mortality of 65 per cent. These figures are a little higher than those given by Ibrahim, who showed a mortality of 46 per cent. of patients treated medically and 54 per cent. surgically. In this connection it may be stated that successful surgical cases are more liable to see the light of publication than those resulting fatally.

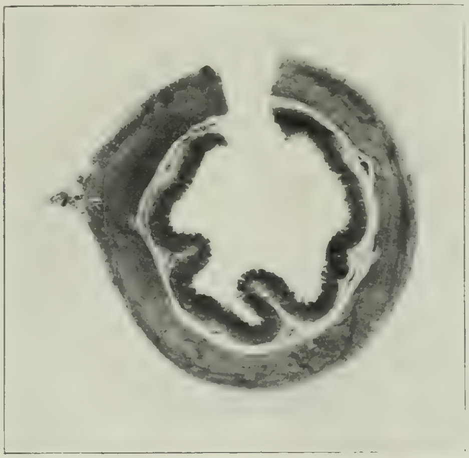

Fig. 19.—Case "X" (Control).—Transverse section of wall of normal pyloric canal. Compare with Fig. 9 (Mag. x 6).

DIAGNOSIS

The diagnosis is not difficult. The history, age of the child, visible peristalsis and other symptoms should at once arouse suspicion. In acute gastric conditions there is always more or less temperature and there is no constipation. It should not be mistaken for dyspepsia from overfeeding, or the habitual vomiting of Finkelstein, in which there is a congenital hyperplasia of the gastric mucosa. The latter condition is caused by too high fat in the food and the vomiting comes on immediately after feeding. True congenital malformations are rare. These are the result of an arrest in development or inflammatory process in fetal life. The baby only lives a few days after birth. The vomitus will contain bile if the obstruction is below the pylorus.

The condition most liable to be confounded is that of functional spasm of the pylorus or pylorospasm. Vomiting is the chief symptom in both these conditions, but in the simple spasm the stools are more frequent and bulky and the child may even have diarrhea. It occurs later in infancy and there is never any marked visible peristalsis and never any palpable pylorus. There may be bile in the vomitus at times.

TREATMENT

The treatment should be individual and each case must be studied intelligently.

The *dietetic* treatment consists in using the breast milk if possible. If the milk is rejected immediately after nursing, it might be pumped from the breast and given in small quantities with a medicine dropper. Some authors advocate giving it ice cold. If the breast milk contains too much fat it can be allowed to stand a few hours and the fat removed and the bottom milk given. Peptonized skimmed cow's milk will sometimes be retained. Whey, malt soup, albumin-water, acid-milk, etc., may also be tried. It is best to give small amounts at frequent intervals. Feeding by gavage should be employed.

The *mechanical* treatment is most important. Washing the stomach out several times a day with cold water removes the contents of the stomach and prevents fermentation and other changes and also tends to relax the muscles of the stomach. Any intelligent mother after a few lessons can perform lavage successfully. In two of our cases the mothers kept this up for many months without any difficulty. The use of hot compresses over the abdomen after feeding has also been recommended.

The *drug* treatment is unsatisfactory. Alkalies can be administered after feeding to reduce the acidity. The use of small doses of atropin, opium or cocain about half an hour before each feeding has been recommended by some authors.

Surgical treatment should be employed when no further good can be done by conservative methods. Surgery has added much to our knowledge of the pathology of this condition. There are several operations recommended to relieve this condition. A posterior gastro-enterostomy seems to be the choice of most surgeons.

SUMMARY AND CONCLUSIONS

1. The pyloric tumor is due to a thickening of the walls of that portion of the pylorus adjacent to the duodenum—the pyloric canal.

2. This thickening is caused by an hypertrophy of the muscle coat, chiefly the circular fibers.

3. The cause of this hypertrophy is not evident.

4. Inflammatory changes may or may not be present.

5. Spasm of the (hypertrophied) muscles, due to local or reflex cause, may be a factor in producing stenosis.

We are indebted to Dr. Ellis Kellert for assistance in the technical work and to Mr. J. A. Glenn for photomicrographs.

361 State Street—143 South Lake Avenue.

ALBUMIN-MILK IN INFANT FEEDING*

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I. LITERATURE

As the logical conclusion of many years of systematic effort to arrive at some definite ideas as to the nature of nutritional disturbances in artificially fed infants, with especial regard to the treatment, in May, 1910, Finkelstein and Meyer[1] first published their results with a new milk combination which, because of its high protein content, they named "eiweissmilch." Their reasons for preparing such a food are best given in their own words.

> "The sugar (or rather, carbohydrate) is to be regarded as the essential and primary fermentation substratum without which as little a normal as a pathological acidification can take place. The fat can take part only secondarily, and then it is dangerous in the sense of acid fermentation only if the fermentation of the carbohydrates has previously begun. The fermentation of the sugar in turn is also dependent on various factors; first, whether the whey concentration is more or less suitable for the intestine, and as a result offers greater or less work for the intestinal epithelium; in the second place, on the proportion of the casein content contained in the mixture to that of the sugar. It is therefore clear that just as in the other rules of nutrition, so in regard to intestinal chemical action, the action of one food-stuff can never be estimated and judged by itself, but always and repeatedly the nature of the processes results from the quantitative proportions and the changing conditions of the whole of the organic and inorganic food-stuffs."

In endeavoring "to combat the dyspeptic fermentations" they decided that the following principles were necessary in the preparation of a food:

> "Reducing the quantity of milk sugar; diminution of the salts by diluting the whey; enriching the casein with a changing, but, under certain conditions, not unmarked fat content; and after improvement is attained, the addition of a carbohydrate easily assimilable and consequently hard to ferment."

To meet these requisites they devised a food which had the following constituents:

Casein from 1 liter milk + ½ liter buttermilk.
Fat from 1 liter milk.
Sugar from ½ liter buttermilk.
Salts from ½ liter buttermilk.

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*Read before the Chicago Pediatric Society, May 22, 1911.

[1] Finkelstein and Meyer: Jahrb. f. Kinderh., 1910, lxxi, 655; ibid 683.

They advised the use of this food in

1. Dyspepsia.
2. Decomposition.
3. Intoxication.
4. Parenteral infections which have led to pathologic conditions in the gastrointestinal tract and therefore to nourishment disturbances of a secondary nature.
5. They wished to convince themselves of its use as a prophylactic for diarrheas in the new-born and very young children in the first weeks of life.

In all, thirty-three cases of dyspepsia were treated. In the beginning, after six hours of tea diet the albumin-milk was given to the amount of 300 c.c. in five to six meals as soon as the stool became normal, which was within three days; in thirty of the thirty-three cases the food was increased to the amount of 100 c.c. every second day until about 200 c.c. per kiloweight was given in twenty-four hours. If the stool was formed there was added Soxhlet's Nährzucker, Liebig's malt-soup or meal to the food. In most cases the decrease in weight had ceased by the third day and the general condition of the child was better. Of the sixteen cases which they were able to follow for an extensive period, only one showed a subsequent nutritional disturbance.

The number of cases of decomposition was thirty-six. The initial tea diet was continued for twelve hours and then the albumin-milk was given to the amount of 300 c.c. per day, the increase being more gradual. It required an average of about ten weeks to bring these children back to a normal tolerance for artificial milk. Of these patients, five died; three of collapse, one of bronchopneumonia and one of influenza. Sixteen infants were treated for intoxication. In these the tea diet was continued for twelve to twenty-four hours, after which albumin-milk was given in the amount of 5 c.c. ten times a day. This was increased rapidly, depending on the stools. A continuance for about eight weeks, on the average, was necessary for complete recovery. Of these sixteen infants, only one died.

Of twenty-six cases of new born, or only a few-weeks-old infants, two died, and in three it was necessary to resort to woman's milk. They do not advise the use of albumin-milk in these cases.

Of twenty-eight cases of severe parenteral infections, such as pneumonia, cystitis, influenza, sepsis, etc., six infants died, and they conclude that the albumin-milk has "an extraordinary influence in maintaining intact the nutritional functions."

Birk[2] soon afterward reported results in thirty mixed cases. In two of his cases the child was taken off of the albumin-milk for cause. In three very severe cases, death followed very soon after the beginning of nourishment with albumin-milk, and in two others death occurred very suddenly while the children were on this food. Birk regards his results as very good. He was not able, however, after a certain time to cause the weight increase to continue in most cases without the addition of carbohydrates, and he is inclined to think that in those cases in which an increase was present without the carbohydrates, it was due to the high milk-sugar content in the food. He regards the food as fitted for intoxications (toxicoses) as well as chronic nutritional disturbances, but had some difficulty in changing from it to other foods. He thinks that the best results can be obtained if the total quantity of albumin-milk used is about one-fifth of the body weight.

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[2] Birk: Monatschr. f. Kinderh., 1910, ix, 140.

Nothmann[3] reported nine cases with one death and regards the use of albumin-milk as almost indispensable.

Contrary to these series of successes is the experience of Chapin.[4] In twenty cases, in which eleven are characterized as atrophic, he had twelve deaths. In all his cases the ordinary percentage method had been previously employed without good results. He naturally is not well pleased with the use of albumin-milk in such cases.

Another article by Abt[5] has appeared, explaining in detail the manner of preparation, indications and directions for the use of albumin-milk.

Braunmüller[6] used albumin-milk in five cases of intoxication with four deaths (one of intercurrent pneumonia). He advises giving sugar only after a long interval, and instead to increase the starches.

Welde[7] reports sixty infants nourished on albumin-milk; these may be tabulated as follows:

Pathologic Condition	Total Cases	Recovery	Unimproved	Deaths
Dyspepsia	25	23	2	0
Decomposition	20	16	0	4
Intoxication	3	2	0	1
Parenteral infections	8	6	0	2
Premature	1	1	0	0
Eczema	3	3	0	0

In concluding he says: "We take the stand that in our home, especially for seriously sick infants, the albumin-milk can no longer be dispensed with." And this in spite of the fact that he had trouble with the irregular composition of the mixture.

In a recent article Finkelstein and Meyer[8] state that failure with albumin-milk is due to the following:

1. Injury to the child through inanition as a result of insufficient doses of the nourishment material in the beginning of the treatment.

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[3] Nothmann: Jahrb. f. Kinderh., 1910, lxxii, 347.

[4] Chapin: Jour. Am. Med. Assn., 1910, lv, 1455.

[5] Abt: New York Med. Jour., 1911, xciii, 121.

[6] Braunmüller: München. med. Wchnschr., 1910, lvii, 2571.

[7] Welde: Therap. Monatschr., 1911, xxv, 83.

[8] Finkelstein and Meyer: München. med. Wchnschr., 1911, lvii, 340.

2. Injury in the beginning of the treatment due to too late or too small carbohydrate addition.

3. Injury by again withdrawing the carbohydrates or by too great reduction on recurrence of the nourishment disturbance in infants which were favorably influenced in the beginning.

They advise a rapid advance in the amount of albumin-milk given to 180 to 200 c.c. per kilo (about three ounces to the pound), or even more, and the increase of the carbohydrates to 5 to 7 per cent.; this increase to consist of Soxlet Nährzucker or Loeflund malt-soup or barley. The carbohydrate should under no conditions be reduced below 2 to 3 per cent., and the food should not be reduced unless the disturbances are severe. Albumin-milk must not be combined with other milk combinations.

II. METHOD OF PREPARATION AND USE

In all the cases reported in this article the albumin-milk was prepared in the infants' diet kitchen of Provident Hospital. The nurses here employed receive, previous to their service in this diet kitchen, a two months' service in the infants' diet kitchen of the South Side Free Dispensary. The albumin-milk was prepared by them in the following manner:

> (1) Buttermilk: The original culture was made from lactone and the succeeding one by inoculation of new milk from a milk culture already twenty-four hours old; it was found advisable to run parallel cultures frequently since at times the original culture would spoil and produce a buttermilk which could not be used; (2) the curds: these were produced by adding a teaspoonful of chymogen (Armour and Co.) to a quart of *boiled* milk; allowed to stand one hour at about 40 C. and then drained through a sterile cheese-cloth bag for one and one-half hours. The curds thus obtained were put through a collander twice; (3) mixing: the curds were then mixed with a pint of buttermilk and water added to make one quart and the whole beaten thoroughly in a small churn.

When this process is completed, the albumin-milk should appear very much as does ordinary milk, except that when the bottle is slightly slanted, fine milk clots will be seen adherent to the glass. The difficulties in the manufacture of this food are many. In the first place, the buttermilk may become poor at any time and render it inadvisable to use it. Second, and a more frequent source of trouble, is the clotting of the curds in the bottom of the bottle in hard masses. To prevent this, several precautions are necessary. The milk after preparation must be cooled and kept cool until time for use; it should not be transported over long distances, but above all, in warming the bottle preparatory to giving the food to the baby, one must only heat it enough to take the chill off the food; in fact, in one of my cases the mother gave the child the food cold without any ill results whatever.

TABLE 1.—RESULTS OF FEEDING ALBUMIN-MILK IN NUTRITIONAL DISTURBANCES

Name	Age[1] (months)	Diagnosis	Time on Alb. Milk (days)	Weight at Beginning (ounces)	Weight at End (ounces)	Average Weekly Gain (ounces)	Time of Ob. Before Alb. (days)	Gain During that Time (ounces)	Results: Immediate	Results: Remote	Carbohydrates: When Added (day)	Carbohydrates: What	Colic	Vomiting	Constipation	Remarks
Roberts	4	Decomp.	10	100	89	—5	39	—29	Bad	Death.	6th	Barley; malt-food.	+	—	—	Death from inanition.
Derlis	7	Decomp.	81	142	209	+5¾	129	—30	Irreg	Good	25th	Malt-food	++	—	—	
E. Burns	8	Dysp.	46	178	199	+3		—	Good.	Good	32d	Malt-food	+	—	+	Left hospital with whooping-cough.
R. Burns	8	Decomp.	153	123	236	+5	—	—	Bad	Good	63d	Malt-ext.	—	—	—	Very severe case of gon. ophth.
Hill	4½	Dysp.	170	141	212	+3	8	2	Good.	Good	7th	Malt-food	+++	+	++	
Sheckel[2]	13	Intox	51	300	317	+2	—	—	Irreg.	Fair	22d	Malt-food	—	—	—	See Note 2.
Voller	2½	Decomp.	45	116	167	+8	—	+	Good.	Good	30th	Malt-food	—	—	+	
Williams	2½	Dysp.	203	144	280	+4⅔	—	—	Good.	Good	28th	Malt-food	—	—	—	
Hank	11	Decomp.	21	204	212	+2⅔	—	—	Good.	Good	7th	Barley	—	—	—	Otitis media and pertussis.
R. Hackett[3]	2½	Decomp.	10	87	78	—6	—	—	Bad	Bad	—	—	+	+	—	Very irregular on E. M.; died two weeks after last seen.
Ruth H.[3]	2½	Decomp.	12	83	83	0	107	—13	Bad	Bad	6th	Malt-food	+	+	—	Died two weeks after last seen.
Ford[4]	7½	Decomp.	87	224	250	+2	—	—	Bad	Good	5th	Malt-food; oatmeal	+	+	+	Very poor reaction for six weeks.
C. Smith	3½	Decomp.	10	123	116	—5	—	—	Fair	Death.	2d.	Malt-ext.	—	—	—	Death.
Olpeter[5]	5	Decomp.	29	143	141	0	—	—	Fair	Fair	12th	Milk-sugar.	—	—	—	
Giffney	3	Decomp.	26	146	154	+2½	6	+ 1	Good.	Good	4th	Malt-food	—	Slight	—	Mother ceased to bring child.
Rome (A)	2	Decomp.	7	126	125	—1	—	—	Fair	Fair	4th	Malt-ext.	—	—	—	Otitis media.
Rome (B)	6¾	Decomp.	51	127	137	+1	—	—	Bad.	Bad	42d	Malt-food	—	—	—	Still under observation[7] May 15.
Dailey[6]	4	....	8	162	150	—12	21	—14	Bad	Bad	4th	Malt-food	—	—	—	Furunculosis of scalp; rickets; death about 1½ months after.
C. Smith	7½	Dysp.	40	170	201	+5	48	+12	Good.	Good	4th	Malt-ext.; malt-food.	+++	+++	—	Still under observation[7] May 15.
McD	1½	Decomp.	61	72	100	+3	42	—16	Good.	Good	23d	Malt-ext.	—	—	—	Developed pylorospasm later.
Bo	2½	Dysp.	7	144	137	—7	—	—	Bad.	Bad	—	—	++	+	+	Developed well on other food.
Hen	4	Decomp.	42	122	124	+ —	30	6	Good.	Fair	3d	Malt-ext.	+	+	—	
Woloscyn	4	Decomp.	11	121	119	—1	—	—	Good.	Good	3d	Malt-food	—	—	—	Still under observation[7] May 15.
Gaston	½	New Born	29	121	131	+2½	—	—	Good.	Good	5th	Malt-ext.	+	—	+	Child in good condition when taken from hospital.
Paetske	7	Decomp.	12	140	132	—4	—	—	Good.	Fair	3d	Malt-ext.	—	—	—	Child in much better condition in spite of loss in weight.[8]
Toomey	3	Decomp.	8	92	81	—8	—	—	Bad	Bad	..	....	—	—	—	Death from erysipelas.

1. Age at time albumin-milk was first given.

2. At first given curds in barley water. Later period of fourteen days on skim milk and skim milk and curds of skim milk.

3. Twins; could not control mother.

4. A very strong suspicion of congenital syphilis in this case. A single convulsion with no return after mercurial treatment. Mother had iritis.

5. Failure due to attempt to introduce whole milk feeding, with loss of six ounces in five days.

6. This child at first seemed well, except for rickets and furunculosis of scalp.

7. Showed distinct improvement, with gain in weight varying from 6 ounces to 28 ounces since last observations recorded in table.

8. Child much worse on other milk mixtures. About one month after the albumin-milk feeding this child developed a scurvy, from which it finally recovered and was in excellent condition.

TABLE 2.—RESULTS OF FEEDING ALBUMIN-MILK IN PARENTERAL AFFECTIONS

Name	Age (months)	Time on Alb. Milk (days)	Weight at Beginning (ounces)	Weight at End (ounces)	Weekly Gain (ounces)	Colic	Vomiting	Constipation	Diagnosis	Results	Remarks
Walsh	6½	82	176	195	1½	—	—	—	Syph. hydroceph.......	No improvement.	Child remained stationary on ordinary milk mixture.
Washington.	6	12	208	218	6	+	+	—	Cong. syph...........	Improved.......	
Spieles	10	7	140	117	—23	—	—	—	Anemia pseudo-infant...	**Death**	R. B. C., 1,900,000; W. B. C., 20,000; Hb., 40 per cent.; Nuc. Red. of all varieties; enlarged spleen.
Graham ...	2½	91	111	101	— ¾	—	—	—	Subcutaneous abscesses.	**Death**	During period when abscesses ceased to form child gained; on recurrence of abscesses child rapidly lost and died.
Gansieca ...	3	11	112	90	—14	—	—	—	Intestinal tuberculosis.	Death	At autopsy ulcers of intestine and rectum; enlarged mesenteric glands; under the microscope many tubercles.

III. COMPOSITION

According to Finkelstein and Meyer, the composition of albumin-milk in comparison with that of cow's milk is as follows:

	Albumin-Milk, Per cent.	Cow's Milk, Per cent.
Protein	3.0	3.0
Fat	2.5	3.5
Sugar	1.5	4.5
Ash	0.5	0.7

Birk states that in the albumin-milk used by him the protein varied from 1.9 to 2.6 per cent.; the sugar as high as 2.5, and once, 3.6 per cent.; on the average, 1.3 per cent.; the fat between 0.9 and 2.7 per cent., usually about 1.8 per cent. He thinks that the variation in the sugar content may account for the fact that "certain children showed unexpected increase in weight with unsweetened milk."

IV. AUTHOR'S CASES

This report consists of thirty cases, of which twenty-five are of nutritional disturbances (Table 1) and five of parenteral affections (Table 2). Of these cases, five were dyspepsias, with four recoveries and one failure; seventeen were decompositions, with two failures and three deaths. Of those classified as failures, both were cases which could not be controlled. Of the deaths, one was the first infant on which the albumin-milk was used and the albumin-milk period was preceded by a long period of decline; one death resulted from erysipelas. In one case of intoxication the infant made a beautiful recovery. In this case a modification of the albumin-milk was used. Instead of suspending the curds in the buttermilk, barley-water was used, and this in turn gradually replaced, an ounce or 2 ounces at a time, with buttermilk. In this case the above procedure did good service. One of the cases in this series was an infant a few days old, of comparatively good health, which thrived well on the food. Another case, aside from a rather severe rickets, and furunculosis of the scalp, showed no disturbance and yet went steadily down hill and died a month or six weeks after leaving the hospital. (Recorded as a death.)

Of the five cases of parenteral affections, three infants died, one was but slightly improved, while one made an excellent recovery. One of those which died had a very severe anemia pseudoleukemica infantum, one was afflicted with subcutaneous abscesses which were very bad at the start and cleared up entirely for some days, then began again and during the second attack the child died. The third was a case of intestinal tuberculosis. The infant which improved only a little was one with syphilitic hydrocephalus; the other case was an ordinary case of congenital syphilis.

SUMMARY OF RESULTS

If we now review these cases we see that in twenty-five instances of nutritional disorder there were eighteen recoveries, three failures and four deaths. Of the deaths, *two* only were uncomplicated nutritional disorders. Of the failures, no infant was on the albumin-milk longer than twelve days, one being taken off the food because of a rather alarming loss of weight in the first week. When it is seen that such a large proportion of my patients were marantic and most of them under 4 months of age, it seems to me that the results are very good.

The cases to which albumin-milk was given were chosen because of their severe character or because of the age of the child. In no mild case in which it was thought that the infant would thrive on the usual milk mixtures was the albumin-milk given. This is shown by the fact that fifteen of the twenty-five cases were in infants 4 months or under.

There are certain symptoms which seem to be peculiarly the result of nourishment with albumin-milk. By most observers a subnormal temperature has seemed to be the rule in the cases of decomposition. This was so only in the more severe of my cases, but did not seem to me to be especially characteristic of nourishment with this food, nor did the addition of the carbohydrates seem to cause any great difference in the temperature curve. Vomiting and colic, with expulsion of flatus, were the rule, though in some cases these symptoms were conspicuously absent. Constipation was very frequent but could usually be controlled by the use of malt-food or malt-extract. The weight usually dropped in the first few days, but responded quickly and soon passed the original mark in the favorable cases. In some, the addition of carbohydrates was necessary to cause a gain in weight, while in others the gain occurred with the albumin alone or diluted with a small amount of thin barley-water.

Quite interesting was the rapid fall and rise of the weight-curve. This occurred usually in the more severe cases and often a drop of 4 to 5 ounces in twenty-four hours would be registered, with a quick return to a point above that before the drop.

Soon after the beginning of the albumin-milk nourishment the child is often pale and the tissue turgor, in instances in which it is possible to estimate it, may be reduced, but these soon come back to the original and I have never seen more healthy artificially fed infants than some of these which I have fed for months on albumin-milk.

In stopping the albumin-milk and changing to some other food, there is frequently great difficulty. If the loss of weight is so great that it becomes a danger to life, no recourse is left except to return to the albumin-milk. It has been my custom to try a milk mixture, always preceded by at least two feedings of barley water. If this produced a rapid loss in weight, I immediately returned to the former mixture. In one case, in which an attempt at mixed feeding was made, my experience was that of others; i. e., that the two forms of food were not compatible.

For the failures here recorded, aside from the outside influences, such as disobedient attendant or parenteral affections, I can find no cause in the composition of the milk or in the absence or presence of carbohydrates. It has seemed to me, however, that a slight diarrhea is not an indication for reduction in the amount of albumin-milk, as it is in other mixtures.

As to why the albumin-milk, when properly made and properly dosed, gives such good results in many almost hopeless cases, it would be difficult to say. This milk as used has no reduction in fat or carbohydrates below the usual milk mixtures. It does, however, contain more protein and less of the salts. The large amount of protein must help to decrease the fermentation in the intestinal canal and thus inhibit one of the most disturbing influences of the carbohydrates.

At present the action of the salts individually and collectively is so little known that it is impossible to draw any conclusions in regard to them. At the same time, indications point strongly to a benefit from their reduction.

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PROTEIN METABOLISM IN INFANTS AND CHILDREN*

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Before going into a general description of nitrogen metabolism it is of the utmost importance to get a general idea of the newer facts known in regard to protein bodies. Protein bodies represent a highly complex organic combination which has become better known through the studies of Hochmeister, Kossel, and especially of Emil Fisher.

The researches of Emil Fisher, Abderhalden, Bergel, Rona and others show that the end-products of the proteins, are the amino-acids obtained by hydrolysis, and are bodies of the normal fat and aromatic series in which the H atom is displaced by an NH_2 group. Of these acids many varieties have been described, of which the better known are glycocoll, alanin, tyrosin, valin, leucin and isoleucin. Whereas the carbohydrate (glycogen) of the body represents combinations of a definite chemical group, the glucoses, and the fats a combination of glycerin and fatty acids, the proteins on the other hand represent many combinations of these amino-acids. We do not as yet classify the proteins by their amino-acid content, if I may use that expression, but according to external properties. Thus we have:

Simple protein bodies.

Complex protein bodies.

The simple protein bodies include the albumins, globulins and the coagulable protein of muscles. These constitute the greater part of the protein in our food and bodies and are what we refer to when we talk off-hand of proteins.

The second group includes mucin, which has a carbohydrate radical attached; the nucleo-albumins, which have a phosphorus group as, for example, milk; hemoglobin, which has an iron group attached, and finally those complex albumins which really perform the functions of our lives, the albumin in the nuclei of the cells, the nucleoproteins, which are made up of purin bodies, phosphorus and carbohydrate groups.

When all these different proteins are ingested, they are split and hydrolyzed by the various ferments in a definite and regular manner. The pepsin reduces them to albumoses and peptones. The end-products (the amino-acids) are not present in the stomach at all or in but small quantities, for pepsin has the property of splitting up the protein body into these more elementary substances only when they are allowed to remain in contact many hours.

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*Read at the meeting of The American Pediatric Society, Lake Mohonk, May 31, 1911.

It is the trypsin of the pancreatic juice, and especially the erepsin of the small intestines, by which these bodies are further split up ultimately into the amino-acids. In the course of this transition there is a period when they are not amino-acids, nor yet peptones or albumoses. In this stage they have been called by Emil Fisher polypeptids and he has actually been able by many combinations of amino-acids to manufacture polypeptids. The end-products of the breaking up of the protein molecule are the amino-acids. The number of these acids is considerable, and it is very likely that there are many combinations and thus many different kinds of proteins of which we have not the least idea. The proteins are absorbed in the form of amino-acids and their combinations. The body has actually been kept in nitrogen balance or even in a plus balance by means of feeding experiments with amino-acids.[1] These amino-acids have also been found in the tissues of the body and serous cavities.[2] The proteins, then, are split up by means of ferments into their ultimate component parts, the amino-acids, then absorbed into the body to be reconstructed into various substances and excreted by the kidneys in the form, principally, of urea and ammonia. As yet the intermediary metabolism, the interval between the absorption of the amino-acids from the intestines and their excretion in the urine and feces, contains many a dark spot which needs further investigation. It is to the end-products which as yet are our only guide that I wish to draw attention in this cursory discussion of the nitrogen metabolism in infants and children.

I shall first discuss the total nitrogen, a consideration of the intake necessary at the various ages, and the nitrogen balance. In discussing this question one must first distinguish between the nitrogen metabolism in the breast fed and in the artificially fed, and above all, not forget to distinguish between the healthy and the sick infant.

A discussion of the metabolism of the breast-fed child is the most satisfactory and easiest, for by comparing the cases in the literature one is certain that the food given was more or less the same, namely breast milk, whereas in the artificially fed one has the difficulty in correlating different percentages of the various food elements, the different quantities taken, and the uncertainty that one is dealing with normal children.

If we take a number of cases of breast-fed babies (see Table 1) from the literature, as Czerny and Keller and Orgler[2] did, adding some of our own, and observe the amount of nitrogen taken in, we will be immedi-

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[1] Schittenhelm and Frank: Ztschr. f. physiol. Chemie, 1909, lxiii, 215.

[2] Umber: Lehrbuch der Ernährung und Stoffwechselkrankheiten, 1909, Urban and Schwarzberg.

TABLE I.—METABOLISM OF BREST-FED INFANTS, SHOWING NITROGEN INTAKE AND NITROGEN BALANCE

Author	Age of Child	Length of Experiment,	Increase in Weight pro die	Nitrogen Food,	Nitrogen Urine,	Nitrogen Feces,	Nitrogen Balance,	Nitrogen,
	Days	Days	gm.	gm.	c.c.	gm.	gm.	per cent.
Michel[4], I	5	3	27	1.52	0.279	0.066	+1.17	77.2
Michel, II	11	3	40	1.87	0.181	0.090	+1.59	85.5
Michel, III	5	4	37	1.462	0.217	0.138	+1.10	75.7
Schwarz[5], IV	4	3	10	1.232	0.188	0.050	+0.994	73.
	Mos.							
Keller[6], VIII, IV	2	5	28	1.875	0.787	0.244	0.843	45.
Michel[7] and Peret[5]	3	3	29	1.675	0.714	0.176	0.785	46.9
Schwarz	4	3	25	1.337	0.626	0.241	0.570	42.6
Schwarz	4	2	12	1.623	0.701	0.164	0.785	46.3
Rubner[8] and Heubner	5	3	85	1.99	1.13	0.40	0.46	23.1

[3] Orgler: Ergebnisse der Inneren Medizin und Kinderheilkunde.

[4] Michel: Recherches sur la nutrition normal du nouveau-ne. Obstetrique. Par., 1896.

[5] Unpublished. Premature weight 1.8 kilo.

[6] Keller: Arch. f. Kinderh., 1900, xxix, 1.

[7] Michel and Peret: Obstetrique, Par., 1899.

[8] Rubner and Heubner: Ztschr. f. Exper. Path. u. Therap., 1905. i.

ately struck with the fact that irrespective of the age, the amounts taken in are about the same.

Thus the 3-months-old child of Michel and Peret or the 4-months-old child of Schwarz does not even take as much as the 11-days-old child of Michel, but in contrast to this, the nitrogen in the urine excreted in this 11-days-old child is 0.181 gm. as compared with 0.714 of Michel and Peret and 0.626 of Schwarz. The intake then is about the same but the output is distinctly different, not alone in the urine but also in the feces. The retention is seen to decrease and the output to increase as the infant grows older.

In order to make a comparison of various cases in the literature we must have certain data to go by. These are (1) the amount retained per kilogram body weight per day and (2) the percentage retained as compared with the amount taken in. This latter is called the utilization figure. The first alone would not be sufficient, for if we gave the infant too little, naturally the retention would be too small. A comparison of utilization alone would give us an incorrect picture, for if we gave too much nitrogen, even though a great amount of nitrogen be retained, the utilization would appear small.

It is only by a combination of the amount retained per kilo a day and the utilization, that a proper idea of nitrogen metabolism may be obtained. If these children are arranged according to their ages (see Table 2) and the amount of nitrogen taken in and retained per kilo weight, it will be seen that the amount of nitrogen retained is quite independent of the amount taken in.

TABLE 2.—AMOUNTS OF NITROGEN TAKEN IN AND RETAINED ACCORDING TO AGES

Author*	M I	M II	M III	Schwarz	K VIII	M and P	Schwarz	Rubner and Heubner
Intake pro kilo N.	0.407	0.425	0.545	0.685	0.430	0.354	0.286	0.205
Retention pro kilo N.	0.314	0.343	0.410	0.552	0.194	0.156	0.143	0.048

*The cases are the same as those referred to in Table 1.

If we compare K VIII with M II we see that with similar intake we have 194 mg. retained in one instance and 343 mg. in the other. If we compare the amount retained and their ages it will be seen that the amount of retained nitrogen is dependent on the age, so that a 14-days-old child retains the most and the 5-months-old child the least. Therefore the amount of nitrogen per kilogram weight required in infancy is apparently about the same, but the amount retained and its proportion to the amount taken in, is according to the age.

Grouping a number of these cases roughly together according to age as shown by Orgler,[3] we have an excellent idea of the utilization of nitrogen in infancy.

Age	Up to 14 Days	2 to 3 Months	5 Months
Retention	0.351	0.153	0.048
Utilization	78.3	40.8	23.1

TABLE 3.—NITROGEN METABOLISM IN THE NEW-BORN

Author	Weight, Beginning to End of Experiment	Age during Experiment, days	Food Given	Intake N, gm	Urine N, gm.	Feces N, gm.	Balance N Retention, gm.	Utilization per cent. N, gm.
Schloss and Crawford[9]	....	1-3	Colostrum	1.512	0.598	0.520	+0.394	26.0
Schloss and Crawford	....	3-6	Colostrum	2.883	0.926	0.141	+1.818	63.0
Schloss and Crawford	....	6-9	Colostrum	2.783	0.922	0.139	+1.724	61.9
Schwarz[10]	....	3-7	Woman's milk	3.388	0.547	0.142	+2.698	99.0
Birk[11]	....	1-5	Colostrum	2.886	1.412	0.524	+0.951	33.
Birk	....	....	Woman's milk	0.696	0.891	0.151	—0.346	0.
Langstein and Nieman[12]*	....	7-10	Woman's milk	1.728	0.603	0.186	+0.939	54.
Michel[4] V	35.50	4	Woman's milk	1.808	0.351	0.061	+1.34	73.0
Michel I	37.30	5	Woman's milk	1.52	0.279	0.066	+1.17	72.2
Michel III	26.80	5	Woman's milk	1.46	0.217	0.138	+1.10	75.7
Birk[13]	30.34	3	Cow's milk	0.897	0.437	0.397	+0.063	7.0
Birk	35.30	5	Cow's milk	3.2	2.116	0.096	+0.993	31.0
Birk	....	0-4	Cow's milk	1.339	1.326	0.620	—0.607	0.
Birk	....	0-3	Cow's milk	0.599	0.378	0.147	+0.075	12.5

*Intake and output for four days from seventh to tenth, inclusive, were added together in order to get above figures. First five days gave a negative N balance.

9. Schloss and Crawford: Am. Jour. Dis. Child., i, 203.
10. Schwarz: Case Rogers—Premature, 3 days old.
11. Birk: Monatschr. f. Kinderh., ix, 180, No. 11.
12. Langstein and Nieman: Jahrb. f. Kinderh., lxxi, 604.
13. Birk: Monatschr. f. Kinderh., x, No. 1.

The nitrogen metabolism of the first few days of life shows such distinctive characteristics that I have deemed it better to discuss this separately and collect the available material in one table. Langstein and Nieman showed that there is a negative nitrogen balance during the first few days when the baby is fed on woman's milk pumped from a well-established lactating breast. In their first case the balance was negative for the first four days; in the second case for the first two days; third case for the first two days, and in the fourth case, a premature baby, it was negative for the first eight days of life. In an infant of Schloss and Crawford's, fed on colostrum, the intake of nitrogen was 1.5 gm., and about 1.1 gm. was excreted in the urine and feces, with a utilization of 26 per cent. Schwarz' case, that of a premature infant, beginning from the third day up to the seventh day of life, can hardly be brought under this heading, for it was not controlled from birth. It was fed on woman's milk and showed a retention of over 2.0 gm. of nitrogen during this time, and a utilization of 77 per cent.

Birk's patient—Case I—was fed on colostrum in a five days' experiment, during which there was a physiologic loss from 3,980 gm. to 3,760 gm. In spite of this there was a retention of 0.951 gm. nitrogen, a utilization of 33 per cent. In a second case there was a retention of nitrogen from the second day of life. His third patient, fed on woman's milk from birth, showed a loss of nitrogen. We see here an interesting physiologic fact, that with a loss of weight there may be a retention of nitrogen in the patients fed on colostrum, and a loss of nitrogen when fed on woman's milk. This shows the value of colostrum, for in Langstein's case this loss is ascribed to a breaking down of protein in the tissues. In two of Birk's patients fed on cow's milk the results varied somewhat, for in Case I there was a loss of 606 mg. of nitrogen and in the second case a retention of 75 mg. of nitrogen. The utilization of the nitrogen in the cases in this table differs somewhat from the general rule given by Orgler previously in being considerably less. This is in part due to the fact that in some of the cases the first few days with low utilization of nitrogen are included with the later days of higher utilization, as might have been done if Schloss' periods had not been separated as shown in the tables. Thus, in the first three days the utilization was 26 per cent.; then 63 per cent., which is nearer to the figures obtained by Michel and Peret. Birk ascribes the low utilization in the babies fed on cow's milk to the large excretion of nitrogen in the urine, which in Michel's cases was one-sixth and one-seventh of the intake, while in the cow's milk babies it was as high as two-thirds of the intake. This he regards as a fundamental difference between the two types of feeding. Yet in Schloss' case during the first three days, 30 per cent. of the nitrogen intake was excreted in the urine, and in Birk's Case I, fed on colostrum, 50 per cent. of the nitrogen appeared in the utilization. From the foregoing it is clear that nitrogen utilization in the new-born needs considerable more investigation.

Before taking up the nitrogen metabolism of the artificially-fed child, it is important to know the effect in the same child of increasing the various food elements in the mixture.

As shown above, in the breast-fed child the amount of nitrogen excreted in the urine is not constant and is of no value except as compared with the intake, being 11 per cent. in Michel's[4] 5-days-old child, and 42 per cent. in Michel and Peret's[7] 3-months-old child. So also the amount of nitrogen in the stools, in the breast and artificially fed varies according to the age and the character of the food. The stools present a special problem, for here the nitrogen may be derived from the food, the intestinal secretions, bacteria or epithelium. The nitrogen content of the stool can be increased by changing the character of the food, thus causing an increased secretion, or perhaps poor assimilation or resorption of the food nitrogen. Because nitrogen is added to the food and an increased amount of nitrogen is excreted in the stools, does not necessarily mean that this nitrogen came from the food, for there may have been more intestinal secretion, epithelium or bacteria excreted. In Schlossman's case Kriesch, as quoted by Orgler,[14] the child excreted 1.22 gm. nitrogen in the feces, with an intake of 6.5 gm. of nitrogen, whereas with an intake of 10.05 gm. nitrogen, excreted only 1.119 gm. Child M IV in Orgler's experiment[15] excreted 0.62 gm. nitrogen in the feces with an intake of 8.1 gm. nitrogen. At another time this infant received 3.3 gm. nitrogen and excreted 0.61 gm. nitrogen, a difference of only 0.01 gm. nitrogen. In one of my experiments a breast-fed baby getting 1.6 gm. nitrogen excreted 0.164 gm. nitrogen in the stools; at another time receiving 1.25 gm. nitrogen, excreted 0.346 gm. or three times the former amount with the same intake. The amount of nitrogen in the food then has very little influence on the nitrogen in the feces.

In hunger there is always a small amount of nitrogen in the stools. A patient of Keller's, examined while on a water diet, excreted 0.0716 gm. nitrogen, or 7 per cent. of the dried feces. In Orgler's case[15] the stools contained 5 per cent. nitrogen (dried feces). In my cases with an intake of 1.47 gm. nitrogen and an excretion of 0.15 gm. nitrogen in the stool, there was 4.5 per cent. nitrogen in the dried feces. In another instance with an intake of 1.252 gm. nitrogen there was an excretion of 0.346 gm. nitrogen in the feces, or 4.3 per cent. of the dried feces. This percentage of nitrogen (about 5 per cent.) to dried stool is fairly constant. If a nitrogen-free diet succeeds a water diet there will be an

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14. Schlossman: Arch. f. Kinderh., 1904, xl, 1.
15. Orgler: Monatschr. f. Kinderh., 1908, p. 135.

increase in nitrogen in the feces. What is most interesting is, that if a little flour, which in itself contains but very little nitrogen, is added to nitrogen-free food, there will be a great increase in the nitrogen excretion in the feces. Such an instance is a case of Rubner and Heubner.[16] With a diet of flour containing 1.02 gm. nitrogen there was 0.45 gm. nitrogen in the stools—almost 50 per cent. of the intake. Therefore, as shown by Orgler, the resorption or the difference between the nitrogen intake and that found in the stools is of very little value, and an increase of protein in the food may have no effect on the nitrogen of the feces.

In the adult when in health and taking the proper amount of food there is just a nitrogen balance, but in infancy, in health, there is a marked retention. This is the great difference in their nitrogen metabolisms, for the latter is a growing organism and needs its nitrogen for its increase in weight and growth. It is very difficult to bring an infant into a state of nitrogen equilibrium, in which he will be excreting as much as he takes in. This can be done by reducing the protein intake sufficiently. This will, however, cause a diet to be given which is calorically entirely below the requirements necessary to retain weight. If we proceed now to add protein, the infant will immediately begin to retain nitrogen, although the food values may be very much below the required amount. This explains the phenomenon of nitrogen retention and no gain in weight. The infant adds to its growth and not to its weight.

To illustrate the effect of the addition of fat to the food, I reproduce in part a table of Orgler's (Table 4).

TABLE 4.—SHOWING THE EFFECT ON NITROGEN BALANCE OF THE ADDITION OF FAT TO THE FOOD

Food	Nitrogen in Food, gm.	Urea N, gm.	Feces N, gm.	Balance, gm.	Nitrogen utilization per cent.
Freund I.,[17] Buttermilk	3.389	2.446	0.278	0.665	19.6
Buttermilk and butter	3.047	2.144	0.311	0.592	19.4
L. F. Meyer,[18] 200 c.c. milk, 800 c.c. barleywater, 16.5 gm. casein, 20 gm. sugar.	3.55	1.799	0.256	1.417	42.2
20.0 gm. same and butter ...	3.6296	1.93	0.202	1.45	40.

From Table 4 it will be seen that when buttermilk alone is given, with a nitrogen content of 3.387 gm. there is a utilization of 19.6 per cent. If butter is added, we have the same utilization of nitrogen. L. F. Meyer's[18] case illustrates the same thing. So that we may conclude that the addition of fat to the food does not save nitrogen and the utilization is the same.

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16. Ztschr. f. Biol., 1899, xxxviii, 315.

17. Freund: Zur Wirkung der Fettdarreichung auf dem Säuglingsstoffwechsel, Jahrb. f. Kinderh., 1905, lxi, 36.

18. L. F. Meyer: Biochem. Ztschr., 1908, xii, 422.

The influence of carbohydrates on the nitrogen metabolism is very marked. From Table 5 it will be seen that when a mixture one-half each of milk and water is given, the child retains 0.2 gm. of nitrogen with a utilization of 9.9 per cent. and on giving the same mixture with the addition of malt in the form of malt-soup we have a retention of 0.4 gm. of nitrogen and a utilization of 17 per cent. This action of the carbohydrates, however, does not work in instances in which the children do not stand sugar well, as shown in an experiment on Orgler's Baby O,[19] in which the addition of sugar caused a marked loss of nitrogen. The saving of nitrogen by sugar is caused partly by the fact that the child does not need to draw on its protein if it has plenty of sugar.

TABLE 5.—(FROM ORGLER). NITROGEN BALANCE AND NITROGEN UTILIZATION ON DIETS OF MILK AND WATER AND MALT-SOUP

Food	Food N, c.c.	Urine N, c.c.	Feces N, gm.	Balance, gm.	Utilization per cent.
½ milk and water	2.672	2.027	0.380	6.264	9.9
Malt-Soup	2.3443	1.4963	0.431	0.417	17.8

This cannot be the only cause, for it can be shown that if a very small amount of barley diluent is added instead of water the retention is increased out of all proportion to the very slight increase of carbohydrate and nitrogen in the barley. The utilization is also markedly increased. Just what this is due to is not known.

The relation of the mineral metabolism to the nitrogen metabolism, according to Orgler, is fairly constant. Designating the amount of ash retained as 1.0, the relation of nitrogen to ash will be seen in Table 6, taken from Orgler.

TABLE 6.—SHOWING THE RELATION OF NITROGEN TO ASH

Michel[4] I	2.1:1
Michel II	1.8:1
Michel IV	1.6:1
Michel and Peret	1.4:1
Rubner and Heubner	1.7:1

This is not the case in artificially fed infants and is especially important in sick children, for whenever alimentary disturbances occur there is a marked divergence from the above.

In a consideration of the nitrogen metabolism of the healthy artificially fed, all the above-mentioned factors must be taken into consideration and one must be sure that the child is absolutely healthy and gaining weight regularly. It is important in the first instance to be oriented concerning the utilization and intake with breast and artificial feeding in the same child in order to determine whether the utilization of

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19. Orgler: Jahrb. f. Kinderh., 1908, lxvii, 383.

TABLE 7.—SHOWING NITROGEN INTAKE, RETENTION AND UTILIZATION IN BREAST-FED AND ARTIFICIALLY FED INFANTS

Author	—— Keller ——		—— Orgler ——		—— Orgler ——		—— Orgler ——		——Schwarz——	
......	(KVIII)		I		II		III		......	
......	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed
Intake, gm.	0.320	0.454	0.221	0.379	0.234	0.498	0.191	0.425	0.295	0.35
Retained, gm.	0.194	0.155	0.076	0.120	0.108	0.148	0.053	0.154	0.144	0.20
Utilization, per cent.	45.	34.	34.	31.	45.4	29.	27.9	36.4	48.8	58.8

nitrogen is the same or better in the one method of feeding than the other. For this purpose Orgler has three cases in sick infants and only one in a healthy breast baby. To this we can add one case in a breast child which was apparently healthy, and was used because its mother had a nephritis and was excreting large quantities of albumin in her urine. The infant also had a faint trace of albumin.

In Table 7 these cases are tabulated. It was unfortunate that in Keller's case the child while on the bottle did not get enough calorically, yet the utilization was almost as good as when on the breast. In comparing Orgler's Case III and Schwarz' case it will be seen that the retention and utilization while on cow's milk may even be better than with breast milk if the artificial feeding is properly conducted. In a comparison of healthy bottle babies to other breast babies of the same age it can be said that the retention and utilization is at least as good. The resorption is also as good in artificial feeding as in the breast feeding, as shown in a case of Orgler's[20] in which an infant getting five feedings a day of woman's milk had resorption of 74.8 per cent. of intake; on two feedings of breast milk and three of cow's milk the resorption was 78.3 per cent. and on a cow's milk mixture calorically sufficient the resorption was 82 per cent.

In the sick infant, the conditions in breast or artificially fed infants are harder to compare, for here the unit of comparison, the kilo, is usually less than in normal children of the same age, and this fact necessitates a comparison with younger children. It is remarkable how much nitrogen these infants will retain while in their convalescence from intestinal disturbances. This pertains also to the artificially-fed child.

Orgler's[21] conclusions concerning nitrogen utilization might well be repeated.

1. Healthy artificially-fed infants show similar or even better figures of nitrogen retention than healthy breast-fed babies of the same age.

2. Retention in the sick artificially-fed child is as good as in the sick breast-fed child.

3. Healthy infants often show better figures for retention when given a proper cow's milk mixture than on the breast.

4. The utilization of nitrogen may be as good or even better in the artificially fed than in the breast fed.

Let us consider for a moment how the functions of nitrogen differ in the adult and in the child.

1. Nitrogen repairs waste; makes good the daily wear and tear of the protein constituents of the tissues, used up in the performance of

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[20] Orgler: Monatschr. f. Kinderh., 1908, vii, 135.

[21] Orgler: Ergebnisse der inneren Medizine und Kinderheilkunde, ii, 509.

their functions. Of course this is equally important to both child and adult, but in the latter it constitutes most of its utility, and in arranging the adult dietary the protein need which shall subserve this function is alone imperative. In infants this minimum protein need, on account of reasons given before, cannot be accurately determined, but in some experiments it seems to run from 0.2 to 0.45 gm. nitrogen during the first fourteen days of life. In an older child a nitrogen equilibrium was struck when given 0.9 gm., being furnished with sufficient calories for its needs by the addition of carbohydrates.

2. Nitrogen adds to the body substance. This deposit or storage of nitrogen plays a secondary rôle in adults, but in children is of prime importance. In adults, under usual conditions, nitrogen is not stored. Any excess administered is split up, burned and eliminated. Only in the hypertrophy of muscles put to special activities, in pregnancy, in convalescence from wasting diseases and after prolonged fasting does such a deposit obtain. In infants and growing children a large part of the nitrogen ingested is added to the body bulk in response to the imperative demand of the impulse of growth. So insistent is this demand that an infant can store nitrogen even when the calories of the food are insufficient. This fact accounts for the common observation that a child will increase in length, though the gain in weight is not essential. In an adult a diet of insufficient caloric value leads to protein loss.

3. The third function of protein is to furnish heat and energy to the body. The heat value of protein is about the same as that of the carbohydrates. Each gram of either substance when completely combusted gives rise to 4.1 calories.

It is not, however, a function for the performance of which the human body looks to protein, but rather to fat and carbohydrates. Moreover, it is not an economical form of fuel when so used, owing to what is termed its "specific dynamic action," some 28.6 per cent. of its value is given off as free heat, leaving only 71.4 per cent. available for the purposes of cell life.

In infants this function of protein plays a small part, especially in natural feeding.

In early life, then, protein is used to repair waste; then to be stored to the limit of the storage capacity of the body; then to furnish energy and be eliminated in the urine.

The sparing of nitrogen built into the body and the storage of nitrogen brought to the body are greatly influenced by the constitution of the food as a whole. Indeed, the art of feeding in infancy, and quite as much in morbid conditions in adult life, depends on this appreciation of the effect of one food stuff on another in the metabolism of each.

As previously stated, the protein taken in is reduced to its ultimate amino-acids, then built up again and excreted mostly in the form of urea and ammonia. It is to a discussion of these, as they make up a part of the total nitrogen in the urine, that we will now turn our attention. It is customary to quote the figures of various constituents of the nitrogen (nitrogen partitions) in the urine, in two ways: first, in actual milligrams excreted in twenty-four hours, and secondly in the amount of each substance as compared with the total amount of nitrogen in the urine.

This urea nitrogen and the ammonia nitrogen constitute the largest part of the nitrogen in the urine. These again, subtracted from the total nitrogen, leave a residue which was previously commonly called the undetermined nitrogen. This undetermined nitrogen is becoming more and more subdivided as we discover new methods of determining quantitatively the products of protein metabolism. At present it can be subdivided into the uric acid nitrogen, purin body nitrogen, creatinin and creatin nitrogen. When all these and the urea and ammonia nitrogen are subtracted from the total nitrogen in the urine, there is still a fraction which is in reality the undetermined nitrogen and is practically identical with the amino-acid nitrogen.

UREA

The formation of the gross urea nitrogen (urea and ammonia nitrogen) excreted in the urine is still an unsettled point. There are probably many ways in which it is formed in the body. That urea is a synthetic product of the amino-acids was long ago definitely established by Schultzen and Nenki[22] and it has been proved that at least one amino-acid, really a diamino-acid, namely arginin, found in the intestine, can be inverted into urea by means of the ferment arginase (Kossel and Dakin[23]). This, however, does not represent all of the urea excreted in the urine. The most probable theory is that the amino-acids have their NH_2 groups split off by desamidating ferments, taken to the liver by the portal circulation, and the liver synthetizes some to urea, the remaining portion being excreted as ammonia. The gross urea therefore represents very probably the desamidating capacity of the organism.

The urea nitrogen according to Morner and Sjoqvist makes up 72 to 76 per cent. of the total nitrogen excreted in the urine. In a year-old child Camerer found the urea nitrogen 72 to 76 per cent. of the total nitrogen, and in a 5-months-old breast baby 83 per cent. of the total nitrogen. In a case of mine a 5-months-old breast baby excreted 0.5 gm. a day, or 72 to 75 per cent. of the total nitrogen, and when put on the

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22. Schultzen and Nenki: Ber. d. deutsch. chem. Gesellsch., 1869, ii, 566.
23. Kossel and Dakin: Ztschr. f. physiol. Chemie, 1904, xli, 32.

bottle this child excreted 0.6 gm. per day or 78 per cent. of the total nitrogen. L. F. Meyer and Ritschel state that the urea coefficient, that is, the percentage of urea nitrogen to total nitrogen, is from 60 to 80 per cent. Hoobler[24] in a presumably normal bottle baby 9 months old, found the urea excretion 52 per cent. when fed on low fats, and 44 per cent. on high fats. This latter is probably due to the fact that there was a compensatory increase in the ammonia nitrogen. In an older child, 5 years of age, the urea nitrogen excretion was found by Schwarz[25] to be 6 to 7 gm. per day, or 87 per cent. of the total nitrogen. According to Folin[26] the amount of urea excreted depends on the nature of the diet. He showed that in cases with a rich nitrogen diet such as eggs and milk, the urea nitrogen can be as high as 87 per cent. and with a nitrogen-free diet may be as low as 60 per cent.

Vogt[27] showed that in acute gastro-enteritis the urea may be as low as 36 per cent. This, however, is not characteristic of acute gastro-enteritis, for a low urea was also found in patients with marked malnutrition without acute intestinal disturbances. They did not seem to do well either on woman's milk or on cow's milk, probably due to an intolerance to fat. This effect of increased fat, or perhaps an intolerance to fat, is shown in Hoobler's case when put on a high fat mixture. Does this low urea excretion mean a disease of the liver? That this is the case in some instances is demonstrated in acute yellow atrophy and phosphorus poisoning in which there is a markedly decreased excretion of urea nitrogen. In gastro-enteritis, however, according to Thiemich,[28] quoted from Vogt, the liver is damaged only in a small percentage of the cases and even in chronic nutritional disturbances there is no great destruction of liver parenchyma. Yet the histologic changes may have no bearing on the ability of an organ to perform its chemical functions.

UNDETERMINED NITROGEN

Before discussing the ammonia nitrogen, I will touch on the question of the undetermined nitrogen in the urine. As stated before, this figure is obtained roughly by adding the ammonia nitrogen to the urea nitrogen and subtracting this from the total nitrogen.[29] In this undetermined nitrogen is included uric acid nitrogen, creatin and creatinin nitrogen, and purin body nitrogen, all of which will be discussed later. This nitrogen is unaffected by the amount of nitrogen ingested and is supposed by Folin and others to be the nitrogen product of a metabolism apart from the other—an expression of the intermediary metabolism. Because of the decrease in the urea nitrogen mentioned above, we have an increase in the undetermined nitrogen, provided the ammonia nitrogen remains constant. Inasmuch as these children with acute and chronic intestinal disturbances are in a state of under-nutrition, it might be said that this diminished urea and high undetermined nitrogen is due to hunger. In adults and in children also, hunger decreases the urea nitrogen, it is true, but there is such a marked increase in the ammonia nitrogen, that when both are added together and subtracted from the total nitrogen we have no increase in the undetermined nitrogen. Vogt examined the nitrogen partition in the urine of new-born infants and was able to find two distinct classes; one with a percentile decrease in the urea and a corresponding percentile increase in the undetermined nitrogen; the other with a high urea and a low undetermined nitrogen. He found, for instance, 46 per cent. urea nitrogen and 44 per cent. undetermined nitrogen as compared with the total nitrogen. In other cases 81 per cent. urea nitrogen and 11 per cent. undetermined nitrogen. Whether this is due to an increase in the uric acid excretion in the one, or to a diathesis, it is impossible at the present moment to say. The increase or decrease in uric acid excretion, however, should not affect the urea; it might, though, make up the greater part of the undetermined nitrogen, and therefore not mean a decreased excretion of the amino-acids in the urine. It is interesting to note that in Hoobler's case on low and medium fats, the undetermined nitrogen was 4.6 per cent. of the total nitrogen, whereas on high fats there was 11.5 per cent. undetermined nitrogen in the urine. Whether this high undetermined nitrogen means a disability of the liver or other organs to form urea from amino-acids, is still an open question. The urea excretion in the many pathologic states in infancy has not been investigated. It would seem especially important to know the excretion of urea in various types of malnutrition. In three cases of rachitic dwarfism Schwarz[30] found the excretion of urea normal as compared with a healthy child.

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[24] Hoobler: Arch. Pediat., 1910, xxvii, 856.

[25] Schwarz: Jahrb. f. Kinderh., 1910, lxxii (Series 3, xxii, part 5).

[26] Folin, O.: Am. Jour. Physiol., 1905, xiii, 45 and 116.

[27] Monatsch. f. Kinderh., viii, No. 2.

[28] Thiemich: Beitr. z. path. Anat. u. z. allg. Path., xx, 179.

[29] I have done this in this portion of my paper because Vogt discusses the nitrogen partitions in the new-born in this manner.

AMMONIA NITROGEN

Since the discovery by Keller[31] that the ammonia nitrogen in the urine of children suffering from alimentary intoxication is greatly increased, intense interest has been manifested in the ammonia excretion in the infant's urine. The ammonia nitrogen co-efficient, that is, the percentage of ammonia nitrogen to total nitrogen, has been the subject of considerable investigation. In a five months' old breast baby Camerer found this co-efficient to be 7.7 per cent.; Keller, 7.7 to 12 per cent. Meyer and Langstein[32] claimed that figures under 10 per cent. are normal. Amberg and Merrill[33] found the ammonia nitrogen co-efficient in breast babies during the first few weeks of life to be from 4 to 12 per cent. During hunger the ammonia output in the urine increases and must not be confounded with an acidosis. Meyer and Langstein have noticed this increase already on the second day of hunger. Folin[26] states that a decrease in the nitrogen intake enough to show a decrease in the nitrogen output in the urine will give an increase in the excretion of ammonia in the urine. Therefore, the ammonia excretion in the normal infant depends on the amount of nitrogen in the food. It has been generally understood that an increase of fat in the food alone caused an increase in the ammonia output. This was shown not to be absolutely the case by Amberg and Merrill,[34] for if the proteins are increased with the increase in the fat there will be no increase in the ammonia output. It depends more or less on the relationship of the fat to the protein. They have shown in a breast-fed baby that if this relationship were kept at 3 to 1 the ammonia output was only 8 per cent. If, however, the fat was increased and not the protein, the ammonia excretion went up to 18 per cent. In Hoobler's[24] case the ammonia nitrogen went up from 2 per cent. on a low fat to 15 per cent. on a high fat mixture, but in this experiment the protein remained about the same, only the fats being increased. From the foregoing it is easily seen that one must be very careful in judging an acidosis by the amount of ammonia excreted. However, the excretion of ammonia in the cases described by Keller went up to 30 or 40 per cent. of the total nitrogen. This is undoubtedly due to an acidosis. It might also be due to a disturbance in the formation of urea, but Keller[35] found that by giving amino-acids such as glycocoll, leucin, and asparagin, there was no relative diminution in the excretion of urea. Pfaundler,[36] on the other hand, thought it might be due to a disturbance in the liver and the formation of urea, on account of the fact that there was a diminished ability of the liver to oxidize salicyl aldehyd. However, the later researches of Stemitz, Keller and Freund proved it to be beyond a doubt due to an acidosis, the increased excretion of alkali taking place through the feces and the ammonia used to neutralize the acids formed.

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[30] Schwarz: Jahrb. f. Kinderh., 1910, lxxii, 724.

[31] Keller: Jahrb. f. Kinderh., 1897, xliv, 55.

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32. Meyer and Langstein: Jahrb. f. Kinderh., 1906, liii, 30.
33. Amberg and Merrill: Jour. Biol. Chem., 1907, iii, 311.
34. Amberg and Merrill: Jahrb. f. Kinderh., lxix.
35. Keller: Centralbl. f. allg. Pathol. u. path. Anat., 1898, ix, 739.
36. Pfaundler: Jahrb. f. Kinderh., liv, 247.

NUCLEOPROTEIN

Before taking up a consideration of the remaining nitrogen constituents of the urine it is important to know something of the breaking down of the nucleoprotein from which a greater part of this nitrogen comes. This nitrogen (uric acid, creatinin, etc.), as contradistinguished from the urea nitrogen, has absolutely no relation to the protein intake. Folin advanced the theory that there are two metabolisms going on, an exogenous and an endogenous. In the exogenous metabolism the organism takes care of the entire intake of nitrogen, with the exception of a small part which goes to the repletion of that nitrogen lost in the endogenous metabolism. This endogenous metabolism is, however, affected by the nucleoprotein intake and it is to this we must now turn our attention.

As stated in the beginning of the discussion, the nucleoproteins are a class of complex proteins and are found in food richly supplied with cells. They are made up of proteins and nucleic acids: Protein *loosely* combined, and protein very *closely* combined, with the nucleic acids, so that when they are taken into the stomach, the pepsin takes the loosely combined protein, forms peptones, albuminoses, polypeptids, and amino-acids. What is left is nucleic acids plus the closely combined proteins, together commonly called nucleins. The trypsin of the pancreatic juice then splits off the protein from the nuclein, and nucleic acids are left. These acids are, no doubt, also split up, but as yet there is only one known ferment that can do so, namely, nuclease, discovered by Sachs[37] in 1905. The pancreatic juice in addition has the property of changing the nucleic acids so as to render them more easily split up. They are broken up in the intestinal wall but not in the lumen of the intestines. Here they are resorbed, but just where they are changed into nucleoprotein of the body is unknown. Perhaps they are taken by the blood stream to the various organs, there combining with the nucleoprotein of the blood, forming the nucleoprotein of these organs. A portion of the nucleic acids is broken down by the intestinal bacteria, for purin bodies are found in the stools.[38] They are derived, no doubt, from epithelium and bacteria.

Nucleic acids when split up result in the following:

1. Purin bases; guanin, adenin, xanthin and hypoxanthin.
2. Pyrimidin bases: thymin, cytosin, uracil.
3. Carbohydrate group (hexoses).
4. Phosphoric acid.

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[37] Sachs, Fritz: Ueber die Nuclease, Ztschr. f. physiol. Chem., 1905, xlvi, 337.

[38] Kruger and Schittenhelm: Ztschr. f. physiol. Chem., 1905, xlv; 1902, xxxv, 153.

Guanin, a purin base, can be converted into xanthin by means of a ferment, and this in turn can be converted into uric acid. Adenin, on the other hand, can be changed into hypoxanthin by means of a ferment, this again into xanthin and then into uric acid.[39] This shows the close connection which these nucleoproteins or nucleic acids have with the formation of uric acid. Jones thinks these changes are due to different ferments (guanase and adenase), but Schittenhelm believes them to be due to the same ferment.

URIC ACID

Uric acid represents the direct metabolism of the nucleoproteins in the food, and it is shown that its excretion is in direct relation to the amount of these bodies ingested. However, if a patient is given a nucleoprotein, or, as it is called, a purin-free diet, he will still excrete a small quantity of uric acid, which is exceedingly constant for the same individual. Burlan and Schur,[40] who first pointed this out, called this the endogenous uric acid. The increased excretion found on giving purin bodies they called the exogenous uric acid. Now, just where does this endogenous uric acid come from? Burean[41] showed that during muscular exercise there is an increased excretion of purin bases in the urine, and soon after of uric acid. He thinks, therefore, that it is formed in the muscles. But it has been shown by Schittenhelm that part of the uric acid thus formed can be destroyed by a ferment which he called the "urikolytic ferment." Therefore, the amount of uric acid excreted is not necessarily all that is formed in the body. If decreased or increased in the urine it can only be interpreted as to whether more is destroyed or less formed. If the former is the case, then the substances into which uric acid is split up should be increased in the urine. Some of these substances, such as glycocoll, oxalic acid and allantoin have been found. A discussion of these, however, would take us too far afield. Yet a search for these substances is of importance as allantoin has been found in the urine of the newly-born by Gusserow.[42]

The excretion of uric acid is especially interesting in the infant, for it receives a food which is purin-free, except during the first few days of life. In order to add nucleoprotein to its body, then, it must be able synthetically to produce these, and it has been shown by experiment on the lower animals that the organism is able to produce nucleoproteins even if kept on a purin-free diet from birth. According to Orgler[43] a breast-fed infant excretes 30 to 40 mg. of uric acid; an artificially-fed one, 70 to 90 mg., the retention being greater in the breast-fed. It makes up about 3 to 5 per cent. of the total nitrogen in the urine.

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[39] Werner, Hugo: Ergebnisse der Physiologie der Harnsäure, 1902, i, Abt. p. 555; Schittenhelm, A.: Die Purinkörper, etc., Ztschr. f. Stoffwechs. u. Verdauungskr., 1904, v, 226; Burean, Richard: Med. Klin., 1905, i, 131; ii, No. 19-21; Mendel: Harvey Society Lecture, Feb. 10, 1906.

[40] Burean, Richard, and Schur, Hyman: Arch. f. d. ges. Physiol. (Pflüger's), Bonn, 1900, lxxx, 241; 1901, lxxxvii, 239; Rockwood: Am. Jour. Physiol., 1905, xii, 38.

[41] Burean: Ztschr. f. physiol. Chem., 1905, xliii, 494.

[42] Gusserow: Arch. f. Gynäk. Berl., 1872, iii, 270.

Table 8.—Uric Acid Excretion in Infants. Total in Three Day Experiments (Orgler)

Food	Uric Acid. .... gm.	Total Purin Bodies, gm.	Uric Acid. .... gm.	Total Purin Bodies, gm.
Breast milk	130.1	137.0	125.	159.3
Cow's milk	201.2	244.6	247.2	288.3
Increased per cent.	54	78	99	82

As noted before, an increase in the nitrogen intake with a purin-free diet does not increase the uric acid excretion. The addition of carbohydrate to the food, however, according to Orgler, reduces the amount of uric acid excreted and there is an increased retention. If this increase in the carbohydrate is continued, the amount of uric acid excreted will increase slightly, but not to the quantity that it was at the beginning of the experiment. As observed before, the addition of carbohydrate to the diet causes an increased retention of nitrogen and with this increased retention of nitrogen an increase in the retention of uric acid, and protein is added to the body with a resulting increase in weight and growth. Were this retention of nitrogen any better in the breast-fed than in the artificially-fed child this might explain the small excretion of uric acid in the former and a correspondingly greater and more steady increase in weight in the breast-fed. Inasmuch as this is not the case one cannot ascribe the greater protein increase to this fact. The nucleoprotein however has a phosphorus and iron group, and it has been shown by Krasnogorsky[44] that the absolute retention of iron is much better in the breast-fed than in the artificially-fed. Orgler thinks this may be the reason that more purin is added to the body of the breast-fed baby than to the one artificially fed, even though the retention of nitrogen is the same. Concerning the uric acid output in the new-born, conditions are somewhat different. Schloss and Crawford[9] have shown that the output is absolutely and relatively high, being greatest in the first three days of life. It is out of all proportion to the amount of purin bases in the colostrum and is greater when the cord is ligated late. They found the excretion to vary from 60 to 100 mg. of uric acid nitrogen per day the first four days of life, 30 to 40 mg. per day in the second four days of life—20 to 30 mg. per kilo weight during the first four days, 8 to 10 mg. per kilo the second four days of life. Uric acid nitrogen made up from 18 to 20 per cent. of the total nitrogen during the first three days of life. Schloss and Crawford seemed to think that the greater excretion of uric acid in the late ligation cases points to the cellular elements of the blood as the origin of this uric acid. This theory is strengthened, perhaps, by the fact that in a case of Schwarz's[45] the uric acid in the urine was greatly increased in a baby 11 days old immediately after a transfusion, being 25 per cent. of the total nitrogen.

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[43] Orgler: Ueber Harnsäure ausscheidung im Säuglingsalter, Jahrb. f. Kinderh., 1908, lxvii, 383.

[44] Krasnogorsky: Jahrb. f. Kinderh., 1906, lxiv.

CREATININ AND CREATIN

The excretion of creatinin and creatin in the urine is still under considerable discussion. Whether one is derived from the other or not, or just where the creatin is changed to creatinin, is unknown. In the adult, creatinin is constantly present in normal urines and creatin is rarely if ever present. During febrile states, or in cases of fasting or in negative nitrogen balance, creatinin may be increased in urine, and creatin may be present in varying quantities, even greater than creatinin.[25] Creatin is normally found in the muscles, which are supposed to be the depot for the body. Creatinin, however, is not found in muscles. The ingestion of creatin does not increase the excretion of creatinin in the urine (Folin[46]). The protein intake does not affect the amount of creatinin in the urine and this excretion is remarkably constant in normal individuals under similar conditions. (Folin, Hoogenhuyze and Verploegh;[57] Wolff and Shaffer[47] and Shaffer.[49]) Folin believes that the creatinin nitrogen co-efficient is an indicator of endogenous nitrogen metabolism, while Shaffer more specifically thinks it is an expression of the endogenous muscular metabolism. Folin further showed that the amount of creatinin excreted depended on the weight of the subject and more explicitly on the amount of muscular weight, or, as Shaffer puts it, "active protoplasmic tissues." In the adult Folin found the creatinin excretion to be 20 to 24 mg. per kilo body weight and Shaffer 18 to 30 mg. per kilo. In a boy of 5 Schwarz found 6.1 to 7.7 mg. per kilo weight—150 to 160 mg. in twenty-four hours. Amberg and Merrell[33] found 26 to 39 mg. excreted in the urine of infants, or 6.7 to 9.9 mg. creatin nitrogen per kilo body weight. These were children beyond the period of physiologic loss. It is

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45. Schwarz and Ottenberg: Am. Jour. Med. Sc., July, 1910.
46. Folin: Jour. Biol. Chem., Am. Jour. Physiol., 1905.
47. Folin, Hoogenhuyze and Verploegh: Ztschr. f. Physiol., xxiii, 1.
48. Wolf and Schaffer: Jour. Biol. Chem., 1908, p. 439.
49. Schaffer: Am. Jour. Physiol., xxii, 445.

especially interesting to note the figures for the first few days of life. This Sedgwick[50] has done in seven cases during the first few days of life. It varied considerably with the amount of urine excreted and as the weight is not included in his table it is impossible to reckon the creatinin co-efficient. The excretion was up to 25 mg. creatinin in twenty-four hours. Sedgwick was further able to demonstrate the presence of creatinin in the amniotic fluid.

AMINO-ACIDS

Embden and Reese[51] and Plaut and Reese[52] found glycocoll in normal urine and only faint traces of other amino-acids. Abderhalden and Schittenhelm,[53] on the other hand, did not find them in the urine unless there was a disturbance in the protein metabolism. Samuely[54] found glycocoll in the normal urine of two new-born infants. Langstein and Reitschel[55] did not find any amino-acids in normal urine. Von Reuss[56] found glycocoll in the urine of infants without relation to age or food. Schultz,[57] using Sorenson's method modified by Frey and Gigon, examined the urine of infants on the breast and on cow's milk, and found 8.5 per cent. amino-acid nitrogen to total nitrogen in the former and 6.7 per cent. amino-acid nitrogen in the latter. These figures are fairly constant for the same child but vary greatly in different children, both in health and disease. In cases of children very much under weight from alimentary disturbances but well at the time of examination, the amino-acid nitrogen in the urine was from 6.7 to 8.5 per cent. In cases of dyspepsia ("Bilanzstörung" of Finkelstein) the amino-acid nitrogen was from 8.5 to 10 per cent.

50 East Ninety-First Street.

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50. Sedgwick: Creatinin Metabolism, Jour. Am. Med. Assn., 1910, lv, 1178.
51. Embden and Reese: Beitr. z. chem. Phys. u. Path. (Hofmeister), vii, 441.
52. Plaut and Reese: Beitr. z. chem. Phys. u. Path. (Hofmeister), vii, 425.
53. Abderhalden and Schittenhelm: Ztschr. f. phys. Chemie, xlvii, 343.
54. Samuely: Ztschr. f. phys. Chemie, xlvii, 376.
55. Langstein and Reitschel: Biochem Ztschr., i, 75.
56. Von Reuss: Wien. klin. Wchnschr., 1909, p. 158.
57. Schultz: Jahrb. f. Kinderh., 1910, lxxii.

A CASE OF INFECTION OF THE NEW-BORN

LOUISE TAYLER-JONES, M.S., M.D.,
WASHINGTON, D. C.

Infections of the new-born are sufficiently common so that the report of a case seems scarcely warranted. On the other hand, the avenue of entrance often cannot be recognized clinically and the case in hand is of interest because the post-mortem examination alone demonstrated the portal of entry; and not only the portal of entry, but the fact that absence of signs in certain cases is of little value.

History.—I was called about 11:30 p. m. April 13, 1911, to see a ten-day-old baby because the left hand had, during the evening, become red and the temperature had risen to 103 F. The history is as follows:

H. B. was born of healthy parents April 3, 1911, and weighed 7 pounds 14 ounces. The labor lasted twelve hours and was normal in every particular, except that the membrane had to be ruptured. The cord was protected in the usual way. The physician on the case is known to be able and extremely careful in every detail, so that infection seemed hardly possible. Icterus, presumably physiologic, developed on the third day and the cord separated on the fourth day, leaving a clean umbilicus. Feedings were regular and normal and the baby seemed healthy in every way. Apparent health continued up to 8 p. m. of the tenth day, when the red area showed on the hand.

Physical Examination.—The general appearance was that of a plump, healthy infant. Aside from the yellow appearance over the flexor surface of the thighs, there was little evidence of jaundice. Everything about the baby, including the spleen, seemed normal except that the lower liver edge was slightly more than 1 inch (2.5 cm.) below the costal margin. The abdomen seemed a little more tense and fuller than normal. The umbilicus was clean and well healed. The skin was everywhere smooth, soft and pink—except for the left foot and hand—like that of a normal, healthy baby. The palm and back of the left hand were red and swollen. This also extended down the whole little finger. The demarkation was elevated and well defined, like that of erysipelas. The left foot showed an oval, red area about 3 by 4 cm. in diameter, shading off gradually into normal skin. This had developed within one-half hour. There was nothing like a bite or scratch to indicate local infection. A diagnosis of infection of the new-born was made. Although another general examination was made, the source of infection was not discovered. The temperature was 103 F., the pulse rate 120 per minute, and respirations 32 per minute and easy. The most recent stool was examined and appeared yellow, soft and well digested.

During the night between midnight and 4 a. m. Friday, April 14, red areas, less marked, developed on the right hand and foot. None of the four areas developed further after 4 a. m. There also appeared during the night a spot on the lower gum on the right side near the median line. This broke and pus exuded from it. From this time the baby began to refuse its food and looked ill. By evening of the 15th he developed convulsions, which continued off and on until he died Sunday, April 16, at 3 a. m., when 12 days old, and just fifty-four hours after the first development of any sign or symptom of disease.

Autopsy.—The autopsy was performed the same morning, eight or nine hours after death. In this short time blood stasis, showing very rapid post-mortem changes, was found all over the body, especially on the trunk and face and upper parts of arms and legs. The umbilicus was apparently clean and healthy on close examination. The abdomen seemed rather full. This was accounted for on section by the large liver. All organs seemed normal except the spleen, liver and pancreas. The gall-bladder was large and empty; cystic, hepatic and common ducts appeared normal.

The liver extended to the anterior superior spine on the right side and sloped up to a point about 2.5 cm. above the umbilicus and 5 cm. below the ensiform process. It was about 3.5 cm. below the costal margin in the nipple line. Weight, 7¼ ounces or 210 gm. (normal about 140 gm.[1]) It was spongy and the capsule pulled off like the skin of an overripe fruit. On section the substance was very dark, with much blood in it. There were some very faintly-marked, illy-defined paler areas of a yellowish tinge. Microscopically the liver showed cloudy swelling and an excessive congestion. There was much acute fatty degeneration, but no apparent connective tissue changes, nor were there any organisms observed. Nuclear degeneration was not noted.

The spleen weighed one-half ounce or 14 gm. (normal 8 gm.[1]) and sections looked very boggy, dark and congested. There were no special changes in the microscopic structure, though the Malpighian corpuscles were obscured. It showed fewer changes microscopically than the liver, but on careful examination some septic thrombi were observed in the trabecular vessels. There were no marked changes in the tissue surrounding the thrombi except possibly in one place a slight hyaline degeneration of recent formation.

Bacteriologic Findings.[2]—Cultures on plain agar, glucose-agar, glycerin-agar, and blood-serum were made. They were taken from the heart's blood, the spleen, the liver and the abscess on the gum; also from the left and right hypogastric arteries. The left hypogastric artery, instead of showing the very dark blood, which had been observed in the other vessels and organs, exuded pus when cut. The right hypogastric artery appeared normal. Cultures were taken from each. Every tube contained a pure culture of streptococcus pyogenes, except that from the gum, which was contaminated with mouth bacteria.

CONCLUSIONS

This baby, which had been apparently perfectly healthy for ten days of its life, died when 12 days old, of a streptococcus infection whose course was by way of the umbilicus through the left hypogastric artery. At no time was there any sign other than perfect health at the navel. It is impossible to say when the infection occurred, but it would seem that the most reasonable presumption would put it at the time of, or soon after, the separation of the cord on the fourth day. The physiologic thrombus of the left hypogastric would probably not be broken down by sepsis for several days, and several more days might be required to have the circulation of the organisms in the blood show evidence by elevation of temperature and external signs. Had it taken place at the time of birth, infection would probably have manifested itself several days earlier because of the organisms passing directly into the blood-current, before formation of the thrombus. The skin lesion, the first manifestation in this case, is, though not unusual, certainly not the usual feature, and the average case is that of the 10-day-old baby dying without apparent reason.

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[1] Morse, John Lovett: Jaundice in the New-born. Boston Med. and Surg. Jour., 1910, clxii, 238.

[2] I was enabled to study the pathologic and bacteriologic findings through the courtesy of Major F. F. Russell and Captain C. F. Craig, of the U. S. Army Medical School.

PROGRESS IN PEDIATRICS

ACUTE INFECTIOUS DISEASES

NOTICE

Circular issued by the American Orthopedic Association and the American Pediatric Society in reference to acute epidemic poliomyelitis, addressed to health authorities and boards of health.

Anterior poliomyelitis is, so far as known, a communicable disease, being communicated from one patient to another and also by means of a third person. It occurs in epidemics and tends to spread along the lines of greatest travel. There is reason to believe that it is prevented from spreading by quarantine, and with the very great prevalence of the disease in the summer of 1910 it is the opinion of this committee that it is essential that it should be made a reportable disease in all states in order that its presence may be detected and its spread guarded against.

Of particular significance are the so-called abortive cases, in which indefinite ailments occur in children in communities where frank paralysis also exists. These abortive cases of infantile paralysis are undoubtedly a source of infection, and their record and study is of much importance. In a community where cases of infantile paralysis occur, cases of illness with sudden onset of fever and meningeal symptoms should be closely watched and regarded as possibly infectious. In such cases even recovery without paralysis does not establish the fact that the case was not abortive infantile paralysis.

All cases of infantile paralysis should be strictly quarantined, sputum, urine and feces being disinfected, and the same rigid precautions should be adopted as in scarlet fever. This quarantine should, in the opinion of the committee, last for four weeks, in the absence of definite knowledge as to when the infection ends. Children from infected families should not be allowed to go to school until the quarantine is abandoned. The transportation or transfer of acute cases in public conveyances should be strictly forbidden. It would be very desirable to adopt provisional quarantine measures in suspicious cases in a community in which an epidemic prevails.

The report of all cases of infantile paralysis to the public health authorities should be enforced by law, and all deaths from this cause should be properly described and registered. A careful study of epidemics by public health authorities is strongly advised.

Robert W. Lovett, M.D., Chairman.
Henry Koplik, M.D.
H. Winnett Orr, M.D.
Irving M. Snow, M.D., Secretary.

The Rockefeller Institute for Medical Research of New York City announces that it will devote its resources very largely during the present season to the study of anterior poliomyelitis (infantile paralysis) and to the treatment of acute cases of this disease in its hospital. Physicians and health officers desiring to co-operate in this investigation may do so by sending information concerning the occurrence and prevalence of this disease, or by referring acute cases to the Hospital of the Rockefeller Institute. Dr. Flexner renews his request of last year that whenever possible a portion of the spinal cord and of the nasopharyngeal mucosa derived from fatal cases of the disease be sent to him. Specimens should be preserved in glycerin and sent by mail to Simon Flexner, M.D., Sixty-Sixth Street and Avenue A, New York City.

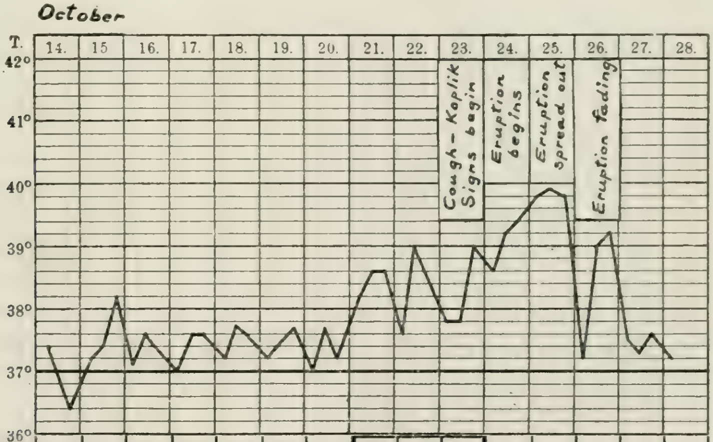
Cytologic and Clinical Observations on the Incubation Period of Measles

(*R. Hecker: Ztschr. f. Kinderh., ii, No. 1, p. 77.*)

In this paper Hecker presents the results of his studies made on fourteen children, five cases, there being two in a family. In the first six cases the leukocytes were estimated, not counted. The specimens were stained with eosin-methylene blue and with azure, the latter method giving the better results, especially in the case of old smears. As a rule 350 cells were counted. The ages

	11. XI.	12. XI.	13.	14.	15.
Clinical Symptoms	Cough		Koplik Signs	Eruption Begins	Eruption Spread
Lymphocytes	26,8	39,0			
Neutrophils	55,7	46,2			
L. Mononuc. & Trans. Cells	8,5	7,8			
Eosinphils	—	—			
Disintegrated Cells	10,7	7,2			
Number of Leukocytes	4200	2400			

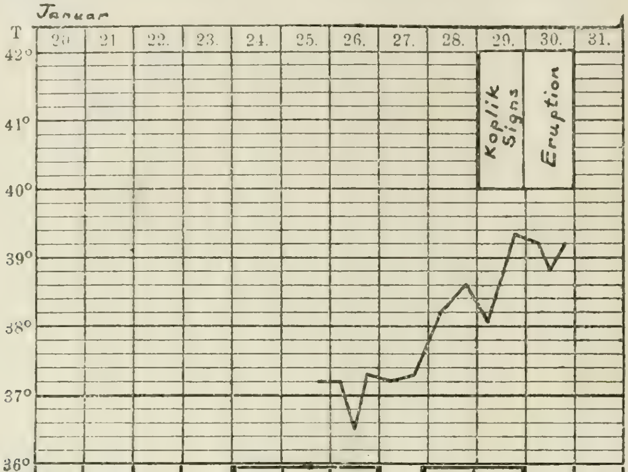
TABLE 1.—Showing clinical symptoms and percentage cell-findings in Fritz U., aged 6 years. The figures framed in black lines call attention to the reversal of the usual proportions of lymphocytes and neutrophils. This applies to the other tables also.



	14.	15	16.	17.	18.	19.	20.	21.	22.	23.	24.	25.	26.	27.	28.
Lymphocytes			59,1	50,4	57,6	51,8	—	29,2	25,1	47,4					
Neutrophils			32,4	38,8	34,5	35,3	—	64,2	61,1	43,4					
Large Mononuc. & Transition Cells			4,9	5,1	1,2	1,0	—	4,2	5,4	5,4					
Eosinphils			0,9	1,2	1,8	0,7	—	—	—	0,4					
Disintegrated Cells			2,2	4,8	6,0	10,3	—	1,6	7,8	8,1					
No. of Leukocytes			7800	7900	10600	6500	—	9100	7000	6100					

TABLE 2.—Showing clinical symptoms and signs, temperature curve (centigrade) and percentage cell-findings in Vera H., aged 5 years.

of the children varied from about two to nine years and all of them had been previously healthy. The results obtained in some of these cases are shown in the accompanying tables. From these tables it is evident that a leukopenia was present, not only during the acute stage of the disease, but also during the incubation period. At times it was only a relative leukopenia while at other times it was absolute and severe. On the average, it was positively noted about three and a half days before the appearance of the exanthem and was probably present as early as four and a half days on the average. It usually appeared even before Koplik's spots were seen, in several cases as early as the fifth, sixth

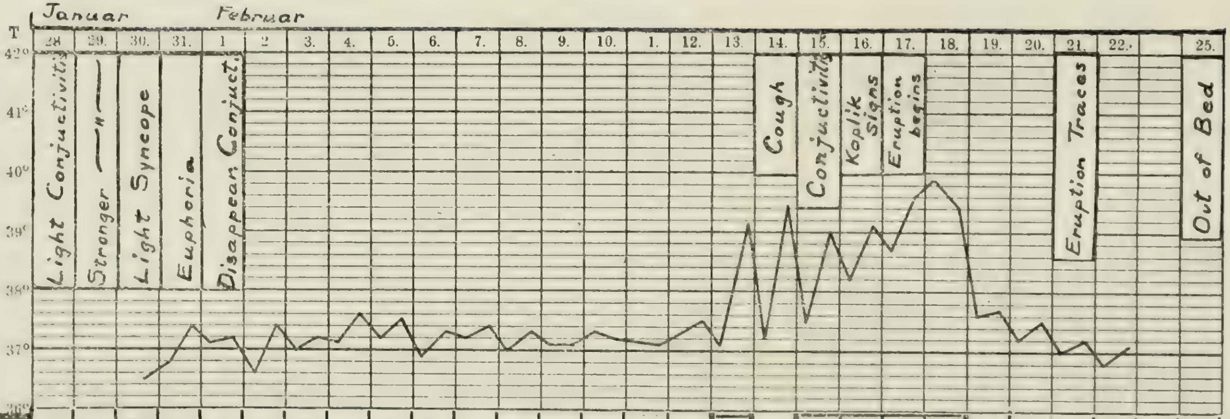


	20	21	22.	23.	24.	25.	26.	27.	28.	29.	30.	31.
Lymphocytes	58.5	62.6	54,0	47,6	39,2	32,8	38,6	53,0	37,1	39,5		
Neutrophils	31,5	26,4	39,9	39,1	44,0	49,0	50,2	42,6	52,9	53,8		
Large Mononuclear & Transition Cells	2,2	6,0	6,1	6,2	6,1	5,2	4,6	1,7	2,4	3,0		
Eosinophils	—	—	0,2	—	—	0,2	—	0,1	—	0,8		
Disintegrated Cells	7,8	4,8	10,0	7,2	10,7	12,6	6,5	2,2	8.0	3,0		
Number of Leukocytes	10000	13000	10000	5000	5000	3000	4000	9000	4–5000	8000		

TABLE 3.—Showing physical signs, temperature curve (centigrade) and percentage cell-findings in Gisela S., aged 1¾ years.

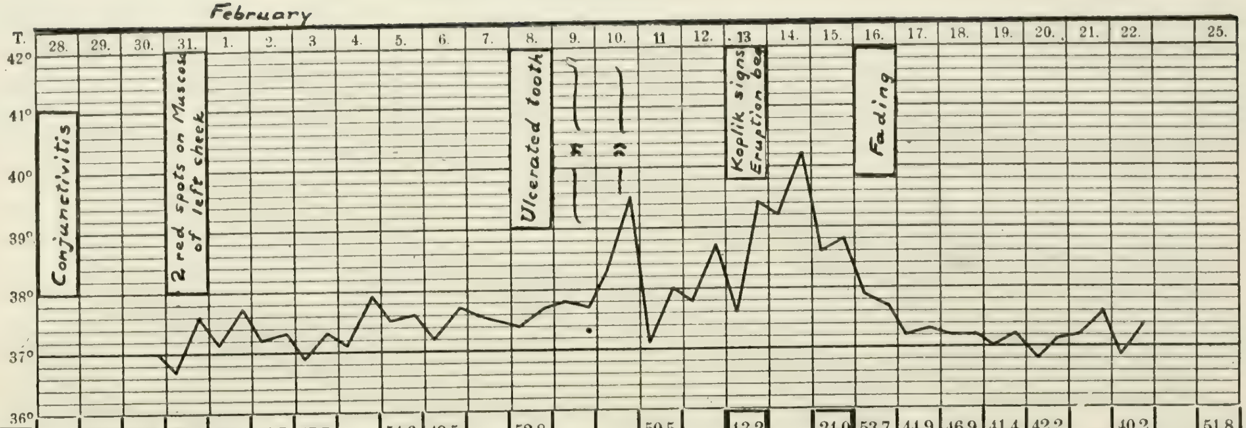
	5. I.		10.	11.	12.		17.	18.	19.	20.	
Clinical Symptoms					Conjunctiv.			Fever, Conjunctivitis, No Cough, No Koplik Signs		Schwindel, abds. Rötung d. Zahnfl., kein Husten	Ausbr. d. Exanthems, nachm. Husten. Etwas Koplik
Lymphocytes	44,7		47,3		45,4		41,1	40,8	45,0		
Neutrophils	45,7		33,7		40,2		49,5	53,1	47,4		
Large Mononuclear & Transition Cells	3,2		4,9		6,5		3,3	3,0	3,0		
Eosinophils	4,9		5,0		6,2		2,9	—	1,3		
Disintegrated Cells	1,1		8,7		1,3		3,0	3,0	3,1		
Number of Leukocytes	14600				17300		9200	8400	7100		

TABLE 8.—Showing clinical symptoms and percentage cell-findings in Hugo C., aged 5 years.



	28	29.	30.	31.	1	2	3.	4.	5.	6.	7.	8.	9.	10.	1.	12.	13.	14.	15.	16.	17.	18.	19.	20.	21.	22.		25.
Lymphocytes		53,3	63,3	55,8	43,5	49,9	57,2		60,9	53,7		58,1			46,2		15,3		24,4	18,8	39,1	23,9	64,0	52,1		45,7		37,7
Neutrophils		43,6	24,8	33,7	26,8	33,2	29,9		36,9	43,1		37,3			40.6		71,8		61,2	62,6	52.5	66,6	12,6	39,6		43.2		57,9
Large Mononuc. x Transition Cells		2,1	7,9	8,1	7,5	7,4	4,7		0,3	1,8		3,5			6,3		7,2		4,0	4,5	1,2	0,8	0,9	2,0		0		12,2
Eosinophils		0,9	1,3	0,8	0,2	0	0,6		0,3	0,3		0,6			0,9		0,6		0	0,5	0	0	0	0,2		0		0
In Disintegration		?	3,0	1,6	22,0	9,2	7,7		2,1	0,8		0,3			6,8		4,3		9,6	13,3	6,3	8,5	21,7	6,0		11,4		0,9
No. of Leukocytes			N	Lets.	N.	Lp.	N.		Lp.	N.		N.			Lets.		Lp.		Lp.		Lp.		Lp!			Lp.		Lets.

TABLE 13.—Showing clinical symptoms and signs, temperature curve (centigrade) and percentage cell-findings in Ingeborg D., aged 6 years.



	28.	29.	30.	31.	1.	2.	3	4.	5.	6.	7.	8.	9.	10.	11	12.	13	14.	15.	16.	17.	18.	19.	20.	21.	22.		25.
Lymphocytes		53,8	56,9	52,3	63,2	41,7	47,7		54,6	49,5		52,8			50,5		43,2		24,0	53,7	44,9	46,9	41,4	42,2		40,2		51,8
Neutrophils		42,5	39,7	47,2	29,4	38,1	50,8		36,7	45,0		40,6			43,8		53,3		66,2	37,2	25,1	29,3	40,5	53,8		48,2		43,7
Large Mononuc. & Transition Cells		1,6	1,6	0,2	4,8	14,2	1,7		3,7	1,8		2,7			3,6		2,4		0,6	3,1	0,6	14,8	12,9	1,4		4,3		1,1
Eosinophils		1,5	0,3	0,2	0	4,5	0,2		5,9	0,5		0,3			1,1		0		0	2,4	1,3	1,4		1,4		1,3		1,7
Disintegrat. Cells		0	0,9		2,8	1,8	0,2		0,7	2,4		3,3			1,1		0,9		9,4	4,6	27,8	6,8	6,1	0,2		5,8		2,7
No. of Leukocytes		N.			N.	Lp.	N.		Lp.	Lp.		N.			Lp.		N.		Lp.	Lp.	Lp.			N.		Lp.		N.

TABLE 14.—Symptoms, signs, temperature curve (centigrade) and percentage cell-findings in Hildegard D., aged 5 years.

Day of Eruption	XVI	XIII	XII	XI	X	IX	VIII	VII	VI	V	IV	III	II	I	Exanth.
1. Fritz U., 6 Jahre												Lp. 4200	Lp. 2400	*	
2. Vera H., 5 Jahre							Lp. 7800	Lp. 7900	Ln. 10600	Lp. 6500		Ln. 9100	Lp. 7000	Lp.* 6100	
3. Gisela S., $1^3/_4$ Jahre					Lcts. 11000	Lcts. 13000	Ln. 10000	Lp. 5000	Lp. 5000	Lp. 3000	Lp. 4000	Lp. 8000	Lp. 5000	Lp.* 8000	
4. Iddy H., $2^1/_2$ Jahre				Ln. 9800		Ln. 9400	Ln. 9300	Lp. 6500			Lp. 7900	Lp. 6000	*		
5. Carola E., 3 Jahre													Lp. 5200	Lp.* 5000	
6. Klemens E., 4 Jahre													Ln. 11000	Lp.* 7700	
7. Erik C., $6^1/_2$ Jahre													Lcts. 12600	Lp. rel. 10000	*
8. Hugo C., 5 Jahre	Lcts. 14600					Lcts. 17300					Lp. rel. 9200	Lp. 8400	Lp. 7100		*
9. Marie Sp., 4 Jahre									Lcts.			Lp.*	Lp.		
10. Anna Sp., 3 Jahre									Lp.			Ln.*	Lp.		
11. Klara B., 8 Jahre							Lcts.		Ln.			Lp.	*		
12. Irene B., 9 Jahre									Ln.				*		
13. Ingeborg D., 6 Jahre	Ln.		Lp.	Ln.		Ln.			Lcts.		Lp.		Lp.	*	Lp.
14. Hilde D., 5 Jahre	Ln.	Lzts.	Ln.	Lp.	Ln.		Lp.	Lp.		Ln.			Lp.		*

TABLE 15.—Number of leukocytes on various days of the eruption in the children examined.
*Appearance of Koplik sign. Lp., Leukopenia. Lcts. Leukocytosis. Ln., Normal number of leukocytes.

and eighth day. On the whole, the leukopenia continued with variations until the eruption appeared. In two cases, however, a leukocytosis was found as early as the second day before the eruption, and in two other cases it was found six and nine days, respectively, before the eruption. Hecker is convinced that the leukopenia is a typical occurrence during the last few days of the incubation period, and therefore it may be considered of diagnostic value in suspected cases. In two cases it was determined that the leukopenia continued five to nine days, respectively, after the appearance of the eruption. The relationship of lymphocytes and neutrophils in the blood count is shown in Table 16. This reversal of relative count between these two types of cells is held by Hecker to be characteristic of the second half of the incubation period of measles. The reason for this occurrence is discussed freely but not conclusively. It is pointed out that it may be due to a diminution in the neutrophils or an increase in the lymphocytes or both. Hecker also found a constant diminution in the number of eosinophils before the appearance of the eruption. Many degeneration forms were also found but no diagnostic significance is attached to them. Summing up these findings, it may be said, then, that in cases of measles there are found during the eruptive stage, and in the latter part of the incubation stage, certain typical changes which precede the Koplik spots by from two to six days and which, in suspected cases, aid in making the diagnosis. These changes are (1) leukopenia; (2) relative and absolute disappearance of lymphocytes; (3) reversal of the normal relationship between lymphocytes and neutrophils or reduction in the number of eosinophils.

Day of Eruption	XVI	XV	XIV	XIII	XII	XI	X	IX	VIII	VII	VI	V	IV	III	II	I	Exanth.		
Fritz U.														27 56	39 46	*			
Vera H.									59 32	50 39	[illegible]	52 35		29 64	25 61	47* 43			
Gisela S.							59 32	63 26	54 40	48 39	39 44	33 49	39 50	58 43	37 53	40 54			
Iddy H.						69 23		63 28		66 31					*				
Carola E															31 55	41* 49			
Klemens E															42 49	43* 47			
Erik C.														35 48		46 51	*		
Hugo C	45 46					47 34		45 50					41 50	41 63	45 47		*		
Marie Sp											35 57			45* 45	32 36				
Anna Sp											51 22			49* 47	21 63				
Klara B									60 38			45 46		33 55	*				
Irene B.											32 57						23 72		
Ingeborg D	44 27	50 33	57 30		61 37	54 43		58 37			46 40		15 72		21 61	19* 63	39 53	24 67	
Hilde D		54 33	57 40	52 47	63 21	42 38	47 51		55 37	60 45		53 40			51 44		13* 53		24 66

TABLE 16.—Showing the relationship between the neutrophils and the lymphocytes in the blood-count in the cases investigated.

* Appearance of Koplik spots. The figures framed in black lines show the reversal of the relative count between lymphocytes and neutrophils in the second half of the incubation period of measles.

F. C. Z.

ACUTE INFECTIOUS DISEASES

Scarlet Fever

(*A. E. Vipond: Canadian Med. Assn. Jour., 1911, i, No. 7, p. 817*)

Having come to the conclusion that the specific organism of scarlet fever would probably be found in the lymph-nodes of the body, Vipond confined his work entirely to the glandular system. April 14, 1911, he obtained from the body of a child 4 years of age (who died of scarlet fever) a number of enlarged axillary and inguinal lymph-nodes, from which he obtained the lymph. This lymph, under strict antiseptic conditions, was inoculated into a slant of agar, blood serum and broth. Within a few hours a mixed growth developed on the different media, part of which proved to be *Staphylococcus aureus;* and part, a raised white growth, which on examination, turned out to be bacilli. This bacillus, when isolated, proved to be of rapid growth, and grew steadily on different media, including dextrose-agar, glycerin-agar, blood-agar, plain-agar, blood-serum and broth. On dextrose-agar a well-developed growth was observed within four hours. May 26, 1911, he examined a boy about 6 years of age, who had been suffering from scarlet fever for a period of six days. The case was typical and the lymph-nodes all over the body were much enlarged. Under strict aseptic precautions, a needle was inserted into an enlarged inguinal node, and a few drops of lymph were drawn off and mixed with a small quantity of sterile water. With this Vipond inoculated various media, with the result that in a few hours' time a luxuriant white growth appeared, covering the whole surface of the medium, which on examination proved to be a pure growth of the same bacillus. A boy 10 years of age, suffering from scarlet fever for a period of five days, was also a typical case, all the nodes being enlarged. Lymph was obtained from an enlarged axillary gland and various media inoculated, when a pure culture of the same bacilli developed rapidly. The next patient was a girl 6 years of age, suffering from scarlet fever. On the fifteenth day of the disease, lymph was extracted from a large, anterior cervical node. After various media were inoculated, a pure culture of the same bacilli was again obtained. A girl, 4 years of age, suffered from scarlet fever for five days. The same method being adopted, a pure culture of the same bacilli was readily obtained. The next was a rapidly fatal case of malignant scarlet fever, in which the rash was by no means typical. Cultures were taken from the different nodes and various inoculated media soon showed a vigorous growth of streptococci, with only a few of the bacilli present. Finally, lymph from an inguinal node was obtained from a case of mild scarlet fever in an adult and blood-serum inoculated. The same bacilli were obtained.

From five cases a pure culture was obtained, two from inguinal nodes, one from axillary nodes and two from anterior cervical nodes. Two were post-mortem cases, one being of a severe type, the child dying from myocarditis, though the bacilli were numerous; while the latter was one of great virulence, and in consequence, the streptococci predominated.

Having obtained the bacillus which he regards as the specific organism of scarlet fever, Vipond decided to inject a broth culture into a monkey, with the hope that the animal would develop scarlet fever. In this he was not disappointed. At the time of inoculation, none of the lymph-nodes was palpable. Within forty-three hours, however, both axillæ presented enlarged nodes. The glandular system being gradually involved, the monkey was also irritable, very thirsty and rapidly lost weight. On the morning of the fourth day, the monkey was very weak and ill, had no appetite, was still thirsty and had a coated tongue. In the forenoon of the fifth day, the animal was still very ill, with a low, weak cry; it was hoarse and had a wrinkled face, a tongue coated with white fur, a congested throat, and presented generally a distressed appearance. On the same day, a red rash was apparent, the lymph-nodes also being very much enlarged. In the afternoon of the same day the monkey was still very ill and weak, the rash persisting, while the tongue was characteristic of scarlet fever; the fur had disappeared from the anterior part of the tongue and left the papillæ exposed and prominent; in fact, a typical strawberry tongue was to be seen. At about 7.30 p. m. the monkey suddenly died. The postmortem showed the monkey to be thin and emaciated, the lymph-nodes in the different regions of the body enlarged, the kidneys enlarged and congested, and the tongue of the same strawberry appearance which had developed during life. Vipond obtained the lymph from the cervical, inguinal, axillary and mesenteric glands of the monkey. Tubes of plain agar and broth were inoculated. The following day, the same bacillus was recovered. Identical results were obtained in the case of several other monkeys. The bacilli have been inoculated into five monkeys and two rabbits. Typical scarlet fever has developed in all, including rash, enlarged lymph-nodes and desquamation. No suppuration in any one instance took place at the point of inoculation. Streptococci would likely have had this effect. The same bacilli have been recovered from the lymph-nodes in each instance, and further, the typical growth has developed on the different media. Vipond also succeeded in producing typical scarlet fever in a monkey and a rabbit by direct contagion from monkeys and rabbits suffering from that disease, and recovered the same bacillus from the inguinal nodes. In all the experiments Koch's postulates have been carried out to the fullest extent. Both the monkeys and rabbits developed the disease. The monkeys used were the *rhesus*, Java and ringtail. The *rhesus* and Java monkeys were much more susceptible to the scarlatina poison than the long-tail variety. The shortest incubation period was two days and the longest five days. The incubation period in the rabbit was three days. The lymphatic nodes as a rule were palpable in thirty-six hours after inoculation.

The bacillus will grow on all ordinary media, the growth occurring in three and a half hours—a most rapidly growing bacillus. The cultures show a growth produced by long bacilli with rounded ends, staining variably with Gram, and occasionally showing a beaded structure, but metachromatic granules are not present. Some cultures show sluggish oscillatory motility. The organism is an active spore former, the spores being endogenous and of the same diameter as the organism. The culture on broth forms an adherent film which tends to sink into the medium; the odor is rather offensive. The agar-culture forms a moist, smooth film, which develops rapidly; the edges are filamentous and the growth tends to become raised and subsequently wrinkled. Pink pigment is ultimately produced. On sugar media it is found to be an acid producer with abundant gas formation (dextrose, 70 per cent. acid, 30 per cent. gas; lactose, 50 per cent. acid, 25 per cent. gas; saccharose, 60 per cent. acid, 60 per cent. gas; maltose, no acid, 40 per cent. gas; mannite, 70 per cent. acid, 70 per cent. gas). Milk is slowly coagulated, with formation of acid. Indol is produced in peptone water.

F. C. Zapffe.

AMERICAN ASSOCIATION FOR STUDY AND PREVENTION OF INFANT MORTALITY

The annual meeting of the American Association for the Study and Prevention of Infant Mortality is to be held at Chicago, Nov. 16-18, 1911. The work of the Association will be transacted partly in small sections devoted to special work and partly in larger meetings of a popular nature. There will be reports on infant welfare work in this country and abroad by Professor C. R. Henderson of Chicago, Dr. Hastings H. Hart, Director Department of Child Helping, Russell Sage Foundation, Assistant Surgeon General J. W. Kerr, U. S. Public Health and Marine-Hospital Service, and others. The sections with their chairmen are as follows: City Milk Supply, Prof. E. O. Jordan, Univ. of Chicago; Continuation Schools in Home-Making, Dr. Helen C. Putnam, Providence; Eugenics, Prof. H. E. Jordan, University of Virginia, Charlottesville; Housing, Mr. Lawrence Veiller, New York; Midwifery, Dr. Mary Sherwood, Baltimore; Nurses' Associations and Social Workers, Miss M. Adelaide Nutting, Columbia University.

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EPIDEMIOLOGIC AND ETIOLOGIC STUDIES OF ACUTE POLIOMYELITIS IN PENNSYLVANIA*

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During 1907 some 200 cases of poliomyelitis developed in a district in the northwestern section of Pennsylvania, extending from 78° 55′ to 80° 15′ west longitude and from 41° to 41° 30′ north latitude. The outbreak apparently began the latter part of July in Elk County and in early August in Venango County, appearing first in Elk County at Ridgway and in Venango County at Oil City; later at Du Bois, in Clearfield County and at Eau Claire in Butler County. In this outbreak the height of the epidemic seemed to be reached the latter part of September and by the end of November the disease was practically stamped out. A small outbreak occurred in Adams County during July and August, 1908. Sporadic cases, only, occurred during 1909.

During the summer of 1910 an epidemic of considerable proportions developed in widely separated sections of the state, reaching a total of 1,076 cases before dying out in the early winter months. The 1910 epidemic began in June in the Lehigh Valley, in July in Lancaster County and in Potter County, and later small outbreaks developed in Westmoreland and Fayette Counties, with scattering cases throughout fifty-five counties. In the Lehigh Valley in the vicinity of the two Bethlehems, Allentown and Catasauqua, the outbreak assumed rather alarming proportions and the same may be said of Lancaster County. In Philadelphia the greatest number of cases occurred in a beautiful section of Germantown, in the northern part of the city, and in a new and rather open section of West Philadelphia, with well paved streets and plenty of shade.

The 1,076 cases reported during the year 1910 were grouped geographically with reference to topography, showing conclusively that elevation played no part, as cases occurred at Philadelphia near sea level in considerable numbers and others were reported in areas fully 2,500 feet above the level of the sea. Similar charting was made with reference to distribution of surface waters, with negative results. The only features of this part of the analysis worthy of mention are that moisture and possibly open water-courses may have played some part in the distribution of the disease.

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*Read in the Section on Practice of Medicine of the American Medical Association, at the Sixty-Second Annual Session, held at Los Angeles, June, 1911.

In classifying cases by geologic formation it seems to hold true that over sand and gravel formation the disease was less prevalent and that it was more prevalent in districts not so favorable for drainage. The character of the surface of the earth in each locality and of the subsoil seems to have been worthy of special note in this relation; and while it is of no distinct value in relation to our present knowledge of the disease, it may be worth recording when making future studies.

We were able to learn nothing of value in relation to the distribution of vegetation other than that the disease was most prevalent after vegetation had reached its height and during the stage when full development of plant life had been reached or passed, the greater number of cases resulting when plant life was on the decline and about the time the harvest season had ended. Possibly fungus growths favored by local death of plants may have furnished a nidus for unusual development of an intermediate host in which the virus may have passed through some stage of its life cycle.

Seasonal distribution shows that the disease is most prevalent during the height of summer and early autumn. This distribution is well shown by grouping reported cases by months of sickening, as follows:

	Cases
January	0
February	3
March	2
April	1
May	4
June	27
July	162
August	336
September	318
October	152
November	52
December	10
Month of onset indefinite in	9

During the 1907 epidemic, the chief of the laboratories spent considerable time in the infected area and secured pathologic materials for laboratory study. Full details of this work will be found in the Department's Annual Report for the year 1907. Research work begun at that time has been continued with slight interruption until the present time. It is doubtful whether monkeys inoculated at that time developed a true poliomyelitis; probably the virus secured was not fresh enough for research work. Bacteriologic studies made at that time were not productive of results.

With the beginning of the 1910 outbreak a branch laboratory was opened in Bethlehem through the cooperation of St. Luke's Hospital, and later a second branch laboratory was opened in the city of Lancaster through the courtesy of the city chemist. A great mass of data was secured, and a number of autopsies were performed. The tissues, together with a number of lumbar punctures, gave us constant material for laboratory study, and as soon as good strains of virus were secured inoculation experiments gave us the disease in considerable numbers of cases in artificially infected monkeys.

In addition to making careful studies of tissues and spinal fluids secured from the bodies of those suffering from the disease and in making careful inoculation experiments with these materials, a vast amount of work was done in studying smears of blood and of nasal mucus. Careful studies of bowel contents and urine were carried out, an offer being made to the physicians throughout the state to study all such materials forwarded to the laboratory, together with an offer to send them shipping containers. It is very gratifying to report that the laboratory staff in carrying out this work have confirmed the published researches on poliomyelitis and our hopes at one time were greatly encouraged by a rather constant finding of a microorganism which we were unable, until recently, to grow in pure culture, in the blood of children suffering with the disease and in the blood of monkeys suffering from this disease.

Details of these reports were published from the laboratory in March, 1911. At that time we claimed nothing more than that the organism was found with great regularity in the stained blood of human and experimental poliomyelitis. The only thing new to add concerning it at this time is its demonstrated motility. We are continuing work with a series of experiments and continually propagating several strains of virus with the hope that at some time we will learn what its etiologic significance may be.

RESULTS OF INTENSIVE STUDY OF 748 CASES

An intensive study was undertaken by the department, resulting in a more or less complete record of 748 cases, giving details of physical conditions of the premises in which the patient sickened, the history of any possible exposure either to human cases of this disease or to domestic animals that may have had paralysis, the notes being so complete as to include possible exposure to flies, ticks, mosquitos, ants or any biting insect; exposure to heat, cold or dampness; exposure through swimming, wading or paddling and exposure to dust. A detailed clinical record was secured from the greater number of these cases giving the duration of the fever, the average range of fever, pulse-rate, date of onset of paralysis; full notes as to other cases in the family or neighborhood, a note of the extent of the paralysis at the height of the disease, and finally a note of the extent of residual paralysis existing several months after all symptoms of acute illness had subsided.

We are very greatly indebted to upward of 600 physicians practicing in the commonwealth for all of these detailed records, the compilation of which would not have been possible but for their loyal cooperation.

Detailed epidemiologic records were forwarded by 605 physicians, covering 748 cases.

528 physicians reported 1 case each
45 physicians reported 2 cases each
17 physicians reported 3 cases each
7 physicians reported 4 cases each
4 physicians reported 5 cases each
1 physician reported 6 cases
2 physicians reported 8 cases each
1 physician reported 10 cases

A few interesting observations may be summarized from the many points developed in this intensive study.

Out of 773 cases of poliomyelitis, fifty-nine gave a distinct history of exposure to previous cases, the sexes being equally divided. Nationality seems to play no particular part in this disease, the vast majority of those contracting poliomyelitis being American-born. Males have more frequently contracted the disease than females. Out of this series of cases 437 were males, and 336 were females. But three of the colored race (two males and one female) sickened. In forty-four instances secondary cases developed in the household.

Other acute illnesses two months prior to the development of infantile paralysis seemed to show but little influence. In three instances whooping-cough existed; in three, intestinal indigestion; in five, measles; in ten, diarrhea; in thirteen, gastro-enteritis; in four, influenza; in nine, tonsillitis; in four, acute enteritis.

Great exposure to heat, cold and dampness was noted in comparatively few instances. Great heat was recorded in sixty-five cases; exposure to cold in twenty-seven; exposure to dampness in eighty-nine.

A total of thirty patients are reported to have met with some minor accident a short time previous to the onset of poliomyelitis.

It was somewhat surprising to find over-exertion reported so seldom, a total of twenty-eight cases being recorded, twenty in the male sex, the exertion often consisting of hard work in the open field.

In nineteen cases a history of automobile riding was noted; in sixteen, swimming; in twenty-nine, wading in open streams; in thirty-seven, paddling in water; in 157 instances the individual contracting the disease constantly ran barefoot.

The prevalence of other diseases in the community during the outbreak of poliomyelitis was not as great as has been reported by some authorities. The diseases of particular moment frequently recorded in infected communities were tonsillitis twenty-five times, gastro-intestinal disturbances forty-seven times.

The date of onset by months is of peculiar interest. Occasional deaths from this disease were recorded during the early months in the year, one in January, two in February and two in April. The disease apparently became more frequent the latter half of June, in each instance in communities where patients had died from the infection at some time during the winter months. In June twenty-four cases were reported; in July 120; in August 262; in September 230; in October 130; in November forty-one; in December ten; a total of 1,076 cases being reported to the department during the twelve months.

By action of the Advisory Board of the State Department of Health, poliomyelitis was made reportable Jan. 7, 1910, general advertisement of the regulation taking place immediately, but individual notices were not mailed to physicians until July, so it is possible that some cases were not reported in the first half of the year. A total of 240 certificates were filed with the department giving poliomyelitis as the cause of death. This mortality shows the disease to have been unusually virulent, even granting that a good many cases may have been missed because it had been so recently made reportable.

The average duration of the fever was about four days. The series of cases studied carefully from the family physicians' notes show that in fourteen cases the fever lasted less than twenty-four hours; in thirty-five, two days; in sixty-eight, three days; in sixty-five, four days; in seventy-two, five days; in thirty-four, six days; in 137, one week and over; in eighty cases, two weeks and over.

The temperature range averaged 99 to 104 + F., the records in twelve cases showing 99 to 100; in fifty-four it was 100 to 101; in 106 cases, 101 to 102; in 147 cases, 102 to 103; in 119 cases, 103 to 104; in sixty-five cases, 104 and over.

The pulse-rate was increased in a large percentage of the cases, the average rate being near 100. In twenty-two instances a record is made of a rate above 150. In a vast majority of the cases the pulse tension is given as high.

In tabulating the symptoms present during the onset and early stage of the illness we find irritability present in 372 cases; stupor in 225; nausea in 343; vomiting in 366; retraction of head in 267; retraction of back in 192; nervous twitchings in 345; convulsions in sixty-one; diarrhea in 159; constipation in 349; retention of urine in 118; incontinence of urine in ninety-seven; insomnia in 291; sleepiness in 244, and sore throat in 101 cases. These symptoms seem to apply with great uniformity to both sexes.

Skin eruption was recorded in sixty-three instances. A scarlatiniform erythema was described several times.

It is worthy of note that the presence of pain and tenderness was recorded in 564 cases of the 773 studied intensively. In a very large majority of the cases pain was most severe in the area of the body later showing paralysis and the pain usually subsided on the appearance of paralysis. A greater number of patients complained of pain in the spinal region alone than in any other area of the body, a total of sixty-nine having pain in this region only. Fifty-one complained of spinal and lumbar pain, and in addition, of pain in all extremities. Thirty-three complained of pain in the lumbar region only, nineteen of pain in the cervical region and a total of thirty-seven complained of pain in the large joints, shoulders, hips or elbows; two complained of it in the left thigh only, three in the right thigh, one in the left hand, one in both feet and one in the right foot only. Abdominal pain was not frequent except as associated with nausea and vomiting.

In a few instances (thirty-four) evidence of insect bites was noted. Particulars of these marks will be found in another part of the paper.

In this series of 773 cases, 142 patients (18.4 per cent.) recovered without paralysis and 294 (71.6 per cent.) recovered with considerable residual paralysis.

The distribution of paralysis when at its height presents some interesting features, the following table showing how frequently the extremities alone were involved:

Extremity	Times involved	Extremity	Times involved
Left arm only	16	Both legs only	120
Right arm only	20	Left hemiplegia	35
Left leg only	74	Right hemiplegia	42
Right leg only	69	All four extremities	78
Both arms only	4		

In addition to the seventy-eight instances in which the four extremities were involved, additional parts were paralyzed as follows:

All extremities and both eyes	Once
All extremities, right eye and right face	Once
All extremities, left eye and neck	Once
All extremities, back and abdomen	Once
All extremities, left face, left eye, neck, back and abdomen	Once
All extremities and both eyes	Once
All extremities, neck, back and abdomen	Once
All extremities, neck, back, abdomen and left face	Once

In addition to the 120 cases having both legs only paralyzed, the following cases had additional parts involved:

Both legs and right face	Once
Both legs, right arm and abdomen	Once
Both legs, back and abdomen	Once
Both legs, right face, right eye and right forearm	Once
Both legs and right arm	3 times
Both legs and left arm	Once
Both legs, right arm and right face	Once
Both legs, right arm and neck	Once
Both legs, right arm, right eye and right face	Once

Crossed paralysis was found as follows:

Right upper extremity and left lower extremity	6 times
Left upper extremity and right lower extremity	5 times

In thirty-four instances one or both legs were paralyzed, either alone or in combination with some other part of the body.

In nineteen the right face was paralyzed twice with only the eye or eye and neck involved, and seventeen cases in connection with some other parts of the body.

The left face was involved in twenty-two cases, always in connection with some other part of the body.

Impairment of intelligence was noted in twenty-nine instances.

Housing conditions show that in 149 instances the individual sickened in a large home; in 219 instances in a medium sized home, and in 164 instances in a small dwelling.

When classified with reference to the number of members of the household the tabulation shows two instances in a family of one; thirteen in a family of two; eighty-six in a family of three; 154 in a family of four; 121 in a family of five; ninety-five in a family of six; sixty-two in a family of seven; thirty-three in a family of eight; twenty-three in a family of nine; twenty-three in a family of ten and over.

With reference to the number of children in the household, the tabulation shows 106 instances in which there was one child; 174 in which there were two children; 110 in which there were three children; ninety in which there were four; fifty-nine in which there were five; twenty-two in which there were six; seventeen in which there were seven; twenty in which there were eight; five in which there were nine; four in which there were ten and over; eighteen in which there were none, with 148 unstated cases.

Out of 773 cases contact occurred as follows:

Certain direct contact with acute case	59
Certain direct contact with abortive case	7
Certain direct contact with chronic case	2
Certain direct contact with acute case by second person	5

Adults exposed escaping paralysis	**1,678**
Children exposed, escaping paralysis	**1,062**
Children sleeping in same bed room with acute case, escaping paralysis	**261**

These figures establish the fact that the danger of transmission from one member of the household to another member of the same household is not great and when we consider the number of instances in which other children slept in the same bed-room with the child contracting poliomyelitis, it seems still more remarkable that so few secondary cases occurred. In 289 instances children slept in the same bed-room, only twenty-four contracting the disease.

In nine instances the disease developed in children after having visited communities where this disease was known to be prevalent. In five cases the possibility of transmission through a second individual seemed probable. These will be given in detail with the case history. In a number of instances suggestive illness occurred in the same household with frank cases of paralysis. A few such cases will be cited with their histories.

Further studies of household conditions showed that in 390 homes doors and windows were screened. In 128 homes sanitary conditions are classified as excellent; in 215 homes as good; in 226 as fair; in sixty-six as bad, with 138 unstated.

Mosquitoes were reported as having access to the house 324 times.

The dwelling stood near a stable or barn in 297 instances; near a poultry house 289 times; near a privy 275 times; and forty-seven times a public garbage dump is reported near the residence. Stagnant water nearby is reported seventy-five times; near open streams in 171 instances; near open drains in 140 instances.

In 410 instances trees are reported in the immediate vicinity of the dwelling; in 122, shrubbery. The particular trees enumerated will be found in a table.

Sanitary plumbing is reported in 277 homes; outside closets in 476.

Household garbage was disposed of to hogs on the premises in thirty-six instances; was burned in thirty-eight; a public system of disposal was reported 231 times; was buried in four instances; thrown on surface of ground 162 times; fed to other domestic animals eleven times.

The water-supply to the household was given as public in 327 instances; well in 194 instances; spring in sixty instances and cistern in thirty-three instances.

The ice-supply was given as natural in eighty-four instances; artificial in 164 instances; none used at all in 322 instances; with 203 unstated.

The milk-supply was given as one cow in 167 instances; breast-fed in twenty-five instances; condensed in five instances; in bottles in 194 instances; in cans in 112 instances; in own receptacles in twenty instances.

Fruits and vegetables used prior to illness in the various households and partaken of by those ill may be well summarized in the following table:

Common varieties	117	Watermelon	2
Cabbage	15	Canteloupe	3
Potatoes	19	Pineapple	1
Lima beans	4	Grapefruit	1
String beans	6	Bananas	51
Peas	10	Oranges	47
Parsnips	1	Peaches	36
Carrots	1	Apples	115
Tomatoes	28	Green apples	1
Corn	8	Plums	20
Parsley	1	Grapes	14
Cucumbers	3	Green grapes	2
Celery	7	Cherries	15
Radishes	9	Berries	21
Onions	17	No vegetables used	116
Lettuce	18	Not stated	55

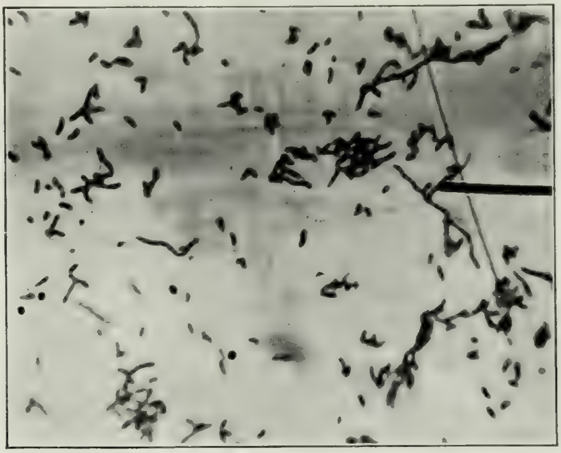


Fig. 1.—Photomicrograph of pure culture of microorganisms found in the blood of patients with acute anterior poliomyelitis, showing long and short forms of the organism.

Vermin were reported as follows:

	Houses
Flies were present in	383
Mosquitoes were present in	212
Mice (house) were present in	149
Rats were present in	77
Ants were present in	85
Roaches were present in	90
Bedbugs were present in	91
Spiders were present in	127
Mice (field) were present in	43
Biting flies were present in	169
Ticks were present in	14

TABLE 1.—POLIOMYELITIS GROUPED BY AGE PERIODS

	Cases		Cases
1 month	2	4 to 5 years	58
2 months	1	5 to 6 years	44
3 months	4	6 to 7 years	50
4 months	4	7 to 8 years	24
5 months	7	8 to 9 years	22
6 months	9	9 to 10 years	20
7 months	12	10 to 15 years	45
8 months	7	15 to 20 years	23
9 months	20	20 to 25 years	18
10 months	7	25 to 30 years	8
11 months	8	30 years and over	8
1 to 2 years	346	Not stated	34
2 to 3 years	187		
3 to 4 years	108	Total	1076

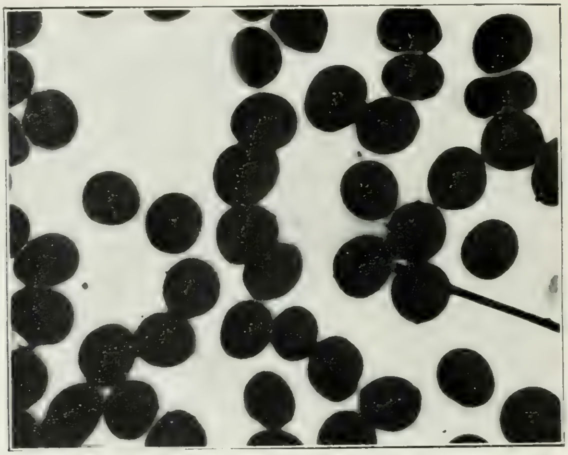


Fig. 2.—Photomicrograph of blood of patient ill of acute anterior poliomyelitis, showing a single organism with bulbous ends connected by a long thin body, attached at one end to red corpuscle in exact center of photograph.

TABLE 2.—DAY OF ONSET OF PARALYSIS

	Cases		Cases
Same day	111	10 days	8
1 day	83	11 days	4
2 days	88	12 days	2
3 days	93	13 days	0
4 days	51	14 days	3
5 days	37	15 days	2
6 days	22	19 days	1
7 days	22	20 days	1
8 days	9	21 days	5
9 days	5	Not stated	126

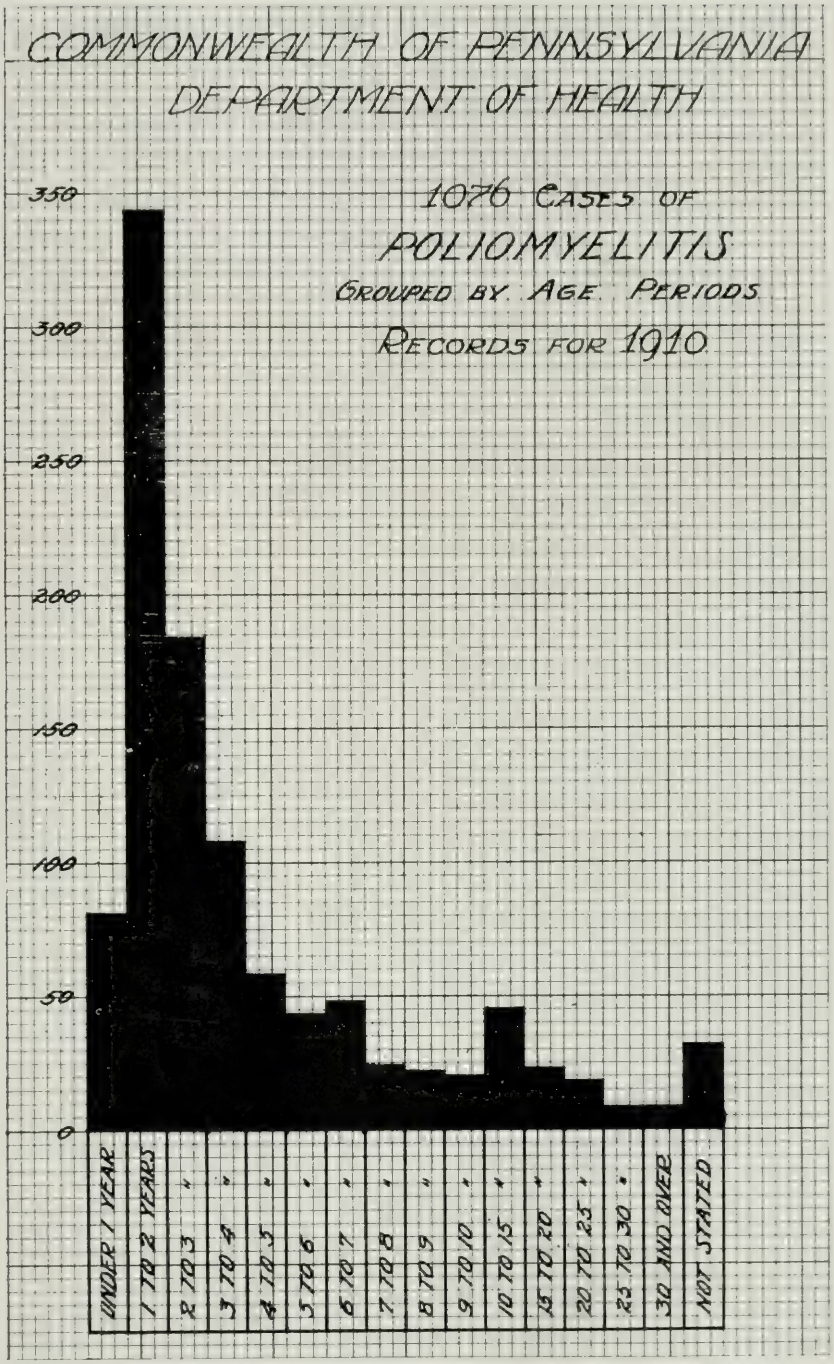


Fig. 3.—Chart showing graphically the cases of poliomyelitis recorded in 1910, grouped by age periods.

Trees and shrubbery stood near the infected house as follows:

Trees	
Fruit	168
Maple	150
Poplar	30
Oak	21
Pine	11
Willow	9
Locust	9
Chestnut	9
Horse-chestnut	9
Elm	4
Beech	4
Walnut	3
Linden	2
Cottonwood	2
Cedar	2
Birch	1
Spruce	1
Shumac	1
Ash	1
Kind not stated	23

Shrubbery	
Roses	26
Grape Vine	10
Lilacs	8
Honeysuckle	6
Hedge	3
Vines	1
Snow-balls	1
Locust	1
Japanese hop vine	1
Cedar	1
Berry	1
Scrub-apple	1
Maple	1
Mock-orange	1
Clematis	1
Underbrush	1
Privet and thorn hedge	1
Kind not stated	52

DATA AS TO DOMESTIC ANIMALS

240 homes had dogs without sickness
264 homes had cats without sickness
254 homes had chickens without sickness
57 homes had birds without sickness
180 homes had horses without sickness
155 homes had cows without sickness
1 home had 1 dog with sickness
3 homes had chickens with sickness (paralysis)
1 home had 1 bird with sickness (paralysis)
1 home had 1 horse with sickness
1 home had 2 cats with sickness

INSECT BITES

Mosquito bites appeared in 15 cases as follows:

Back	1	Body	1
Hands	3	Thighs	1
Face	4	Chest	1
Neck	3	Location not stated	1

Bedbug bites appeared in 2 cases as follows:

Thighs	1	Chest	1

Unknown insect bites appeared in 17 instances as follows:

Face	4	Thighs	2
Neck	2	Temporal region	1
Body	4	Location not stated	3
Head	1		

In many histories rats were reported on the premises. Field mice were frequently found. In 149 homes house mice were prevalent; in 383 homes ordinary flies were found; biting flies were reported 169 times; bedbugs ninety-one times; roaches ninety times; ticks fourteen times; ants eighty-five and spiders 127. Mosquitoes were noted in 212 instances.

Unusual insects were reported in eighteen instances, particulars being found elsewhere.

In three instances paralytic disease occurred in animals, the particulars being set forth elsewhere.

The underclothing worn by those sickening is reported as being cotton in 304 cases; woolen in eighty-two; half cotton and half wool in ten. The stockings were reported as being cotton in 300; woolen in seventy-eight; half cotton and half wool in six.

Several centers of unusual prevalence were noted, one in the vicinity of Galeton near the line between Potter and Tioga Counties, at a great elevation in the northern part of the state; one in the vicinity of the Bethlehems and Allentown in Northampton and Lehigh Counties in the east central section of the state; one in Lancaster County in the city of Lancaster and adjacent rural districts in the south central part of the state and one each in Luzerne and Westmoreland Counties in the southwestern section of the commonwealth, and in Philadelphia county in the section of the city known as Germantown and in a part of West Philadelphia west of the Schuylkill River. The disease was found, however, in fifty-eight counties out of sixty-seven. Grouped by counties the following table shows the distribution throughout the state:

TABLE 3.—SHOWING DISTRIBUTION OF CASES AND POPULATION

County	Cases	Population	County	Cases	Population
Adams	0	34,319	Lancaster	150	167,029
Allegheny	89	1,018,463	Lawrence	4	70,032
Armstrong	7	67,880	Lebanon	3	59,565
Beaver	17	78,353	Lehigh	101	118,832
Bedford	1	38,879	Luzerne	15	343,186
Berks	26	183,222	Lycoming	4	80,813
Blair	0	108,858	McKean	15	47,868
Bradford	4	54,526	Mercer	2	77,699
Bucks	27	76,530	Mifflin	4	27,785
Butler	14	72,689	Monroe	6	22,941
Cambria	3	166,131	Montgomery	33	159,590
Cameron	2	7,644	Montour	1	14,868
Carbon	10	52,846	Northampton	140	127,667
Centre	4	43,424	Northumberland	7	111,420
Chester	11	109,213	Perry	5	24,136
Clarion	0	36,638	Pike	1	8,033
Clearfield	1	93,768	Potter	9	29,729
Clinton	0	31,545	Schuylkill	15	207,894
Columbia	7	48,467	Snyder	1	16,800
Crawford	1	61,565	Somerset	7	67,717
Cumberland	4	54,479	Sullivan	0	11,293
Dauphin	11	136,153	Susquehanna	0	37,746
Delaware	16	117,906	Tioga	19	42,829
Elk	2	35,871	Union	1	16,249
Erie	8	115,517	Venango	4	56,359
Fayette	19	167,449	Warren	1	39,592
Forest	0	9,435	Washington	21	143,680
Franklin	6	59,775	Wayne	3	29,236
Fulton	0	9,703	Westmoreland	50	231,304
Greene	1	28,882	Wyoming	2	15,509
Huntingdon	1	38,304	York	6	136,405
Indiana	5	66,210	Philadelphia	143	1,549,008
Jefferson	2	63,090			
Juniata	0	15,013		1076	
Lackawanna	4	259,570			

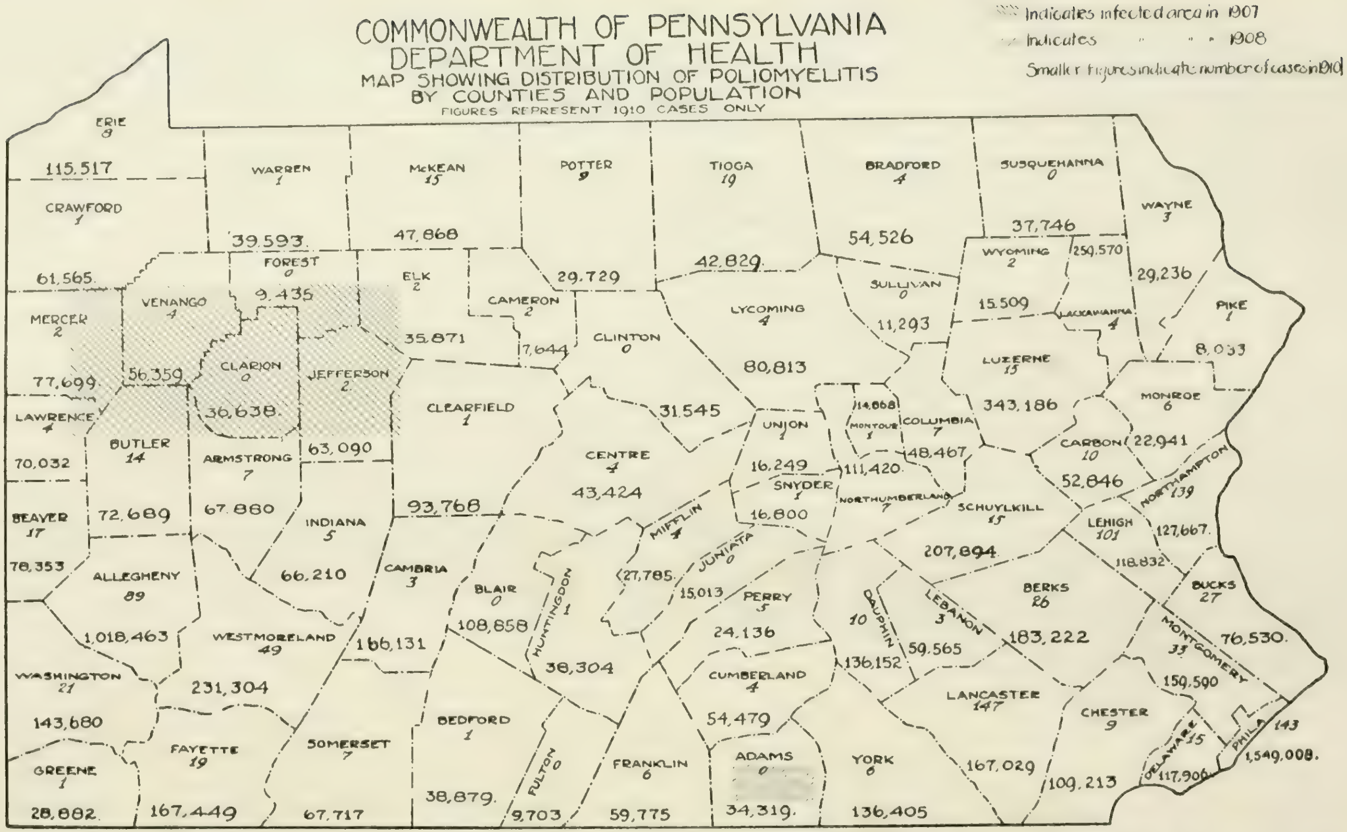


Fig. 4.—Map showing distribution of the disease, and also the population of the counties. The area indicated by broken black lines shows the district in northwestern Pennsylvania affected in 1907 and the district in Adams county affected in 1908.

It is interesting to note that few cases developed in Elk, Venango and Clearfield Counties, where epidemics were reported in 1907, and in Adams County, where a small outbreak occurred in 1908. The exception, however, occurred in Butler County, where a few cases developed in 1907, and fourteen cases in 1910.

The laboratory staff, working from the branches opened in the field, made an intensive study of seventy-three cases during life and a study of pathologic materials from eleven fatal cases, doing a great deal of routine work resulting in statistics too elaborate to refer to more than incidentally in this paper. A composite table of blood-counts alone, when grouped by day of disease on which count was made, is worthy of reproduction.

Day	Polynuclears	Small Lymphocytes	Large Lymphocytes	Eosinophils
2nd to 5th	52.2	34.2	10.1	3.5
6th to 9th	47.2	34.6	13.2	5.
After 10th	51.4	32.8	13.1	2.7

Ordinary leukocyte counts were made in a series of cases. The results seem to show a high degree of leukocytosis up to the ninth day of illness. Spinal fluids were studied eleven times, in each instance fluid being secured during the active stage of the disease. Neutral broth cultures showed the common diplococcus in every such fluid, but in no instance were we able to secure paralysis by inoculation with this organism.

A very large number of swabbings from the nasopharynx were secured and from fourteen such swabbings attempts were made to inoculate five monkeys by applying the centrifugal sediment resulting from macerating these materials in salt solution, swabbing the sediment over the mucous membranes and as nearly as possible placing sediment over the cribriform ethmoidal plate. All of these results were negative.

Six monkeys and seven rabbits injected under the skin with this material gave negative results. These findings seem to show that there is not great danger from the discharges, even though we do succeed in producing the disease by using the actual mucous membranes in the nasopharyngeal area.

Inoculation experiments made in an attempt to produce immunity in monkeys was to a very high degree successful. Attempts to give the disease to rabbits was only in part successful, as we failed absolutely in our attempts to transmit the disease from the rabbit developing paralysis to other rabbits or back to monkeys. It is possible that failure in this experiment occurred because the paralysis in the rabbit was not demonstrable until two weeks after inoculation.

In several communities an unusual number of yellow butterflies were reported. A series of these butterflies were collected, killed and macer-

TABLE 4.—SHOWING DETAILS OF CONTACT CASES

No.	Name	Contact	Manner	Same House	Date of Contact	Onset of Paralysis
160	J. Z.	From Trenton, N. J., direct contact in Lancaster on July 19. Indirect contact through father July 20	Direct and Indirect	No	July 19-20	July 20
20	H. H.	E. V. Philadelphia	Direct	No	3 yrs. or less	July 1
733	L. H.	D. F.	Direct	No	July 14	July 23
315	C. S.	N. D.	Direct	No	Aug. 24	Sept. 1
188	J. C. S.	H. G., New Brighton	Direct	No	Aug. 21	Sept. 1
1	M. M.	M. M.	Direct	No	July 27	Aug. 10
34	C. D.	K. L.	Direct	No	Aug. 26	Sept. 9
17	M. C.	H. T.	Direct	No	July 10	Aug. 24
715	A. E.	G. E.	Direct	Yes	Sept. 1	Sept. 10
499	F. O.	Case in same house	Direct	Yes	Aug. 5	Aug. 25
319	W. R.	Brother	Direct	Yes	Unstated	Aug. 9
577	C. H.	Brother	Direct	Yes	Aug. 25	Sept. 3
296	J. N.	Several cases in Scranton	Direct	No	July 3	July 10
492	W. G.	1619 Chew St.	Direct	No	July 10	July 12
501	J. K.	Neighbor	Direct	No	July 12	July 26
255	B. W.	S. H.	Direct	No	Aug. 18	Aug. 25
390	L. E. L.	Child. Smock, R. F. D.	Direct	No	Oct. 19	Nov. 2
670	J. S.	Philadelphia (L. children)	Direct	No	June 21	July 1
700	N. Y.	A. Y.	Direct	Yes	Constant	Sept. 27
704	W. Y.	A. Y.	Direct	Yes	Constant	Sept. 30
691	F. C.	E. F.	Direct	Yes	Constant	Aug. 7
696	S. B.	K. B.	Direct	Yes	Oct. 8	Oct. 11
693	H. R.	H. R., N. Bethlehem	Direct	Unstated	June 20	July 7
847	F. S.	Other case in family	Direct	Yes	Unstated	July 25
846	R. S.	F. S.	Direct	Yes	July 25	July 29
446	M. U.	J. C. (Slept in same bed) No. 527	Direct	No	June 15	June 26
261	M. H.	W. H.	Direct	Yes	July 24	Aug. 1
268	L. M.	Case 1067	Direct	Yes	Constant	Aug. 15
239	G. C.	K. C.	Direct	Yes	Constant	Sept. 11

610	L. H.	N. H.	Direct	Yes	Aug. 17	Aug. 24
94	A. R.	M. R.	Direct	Yes	Oct. 31	Nov. 4
234	M. O.	C. O. (Case 554)	Direct	Yes	Constant	Sept. 3
329	F. O.	C. O. (Case 554)	Direct	Yes	Constant from 8/23	Sept. 2
342	M. W.	R. W. (Case 338)	Direct	Yes	Constant	Sept. 19
666	W. A.	Brother (Case 665)	Direct	Yes	Aug. 24	Sept. 8
602	M. H.	Brothers and sisters	Direct	Yes	Aug. 1	Aug. 7-8
585	C. E.	Sister	Direct	Yes	Aug. 1	Aug. 8
434	D. G.	Child from Huttles, Pa.	Direct	Yes	July 15	Aug. 11
743	H. W.	While waitress served a baby short time before who died from disease	Direct	No	Unstated	Oct. 5
1040	P. S.	Brother	Direct	Yes	Aug. 2	Aug. 9
2	M. M.	Visit of mother to other case	Indirect	No	Sept. 24	Oct. 13
393	P. C.	Grandmother from Lancaster ten days prior former contact with case	Indirect	No	Sept. 21	Oct. 1
606	— D.	Mother ironed Huber family wash. Case 602	Indirect	No	Aug. 1-8 inc.	Aug. 12
269	B. T.	Cases in neighborhood	Indirect	No	Unstated	Sept. 15
231	A. H.	Cases within a mile	Indirect	No	Unstated	Aug. 1
201	N. K.	Came from Trenton week previous to June 5	Indirect	No	Unstated	July 7
27	D. A.	Other case in neighborhood	Indirect	No	Unstated	Aug. 5
234	N. H.	Visited Lancaster Co.	Indirect	No	Sept. 25	Oct. 1
109	A. S.	Colerain Twp. Lancaster Co.	Indirect	No	About Aug. 1	Aug. 18
304	J. D.	In Pottstown prior to Sept. 24. In Elizabeth from Sept. 24 to 26	Indirect	No	Prior to Sept. 26	Oct. 1
657	J. C.	Allentown on or about Sept. 20	Indirect	No	Unstated	Oct. 1
325	C. W.	B. family	Indirect	No	Unstated	Sept. 20
357	F. T.	R. M. milk from M. cow	Indirect	No	Constant and Unstated	Oct. 14
385	E. Y.	M. case	Indirect	No	Unstated	Nov. 4
184	M. B.	Philadelphia	Indirect	No	Unknown	Aug. 8
363	B. S.	J. S. Brookville, R. D.	Unstated	No	Aug. 1	Dec. 1
403	M. B.	S. V. Snedekerville, Pa.	Unstated	No	Sept.	Oct. 1

ated. Inoculation experiments from the resulting material failed uniformly to produce paralysis.

In the Bethlehems a blight among Norway maple trees attracted considerable attention and it was thought by many citizens that this disease was more prevalent near houses where cases of poliomyelitis existed. A careful examination of these conditions showed that the blight was not confined to the Norway maple and that there was no greater involvement of trees in the vicinity of the affected houses than elsewhere. Examination of the blighted branches showed a delicate mycelium running through the mesophyl of the leaves that was not identical with the oidium of Westphalia. The study of this mycelium gave us negative results. A large number of specimens of blood smears, samples of feces, urine and nose and throat swabbings were sent us by practitioners, but aside from finding microorganisms in the blood with great uniformity, nothing worthy of note was seen.

EXTRACT FROM LABORATORY REPORT PUBLISHED MARCH 2, 1911

In examining the blood from acute cases of poliomyelitis in human beings, and also in monkeys in which the disease was produced experimentally, an organism was found, different in morphologic characteristics from any heretofore described which may or may not, on further investigation, prove to be the etiologic factor in the causation of the disease. Blood smears being fixed in methyl alcohol for one minute and stained with carbol-thionin, the organism appears as a faintly-stained blue rod with regular cell wall about 10 microns long and about 8 microns in width, curved at an angle of 60 to 75 degrees at one end, occasionally at both ends. At times, the curved end is bulbous. Some of the organisms appear to have a very finely granular protoplasm when the highest amplification is employed. They may be discerned by means of a 4 mm. dry objective but their characteristics are much more satisfactorily delineated under the 1/12 oil-immersion lens. They are found free in the serum as well as within the body of the red blood-cell.

The organisms do not retain the violet color when stained by the method of Gram but assume the color of the counter stain which, as generally used in this laboratory, is a very dilute solution of carbol-fuchsin.

The bloods examined were from ten different cases of acute poliomyelitis in children and were taken during the epidemic of last summer and autumn, and from thirteen cases of the disease during the acute stage, which had been produced experimentally in as many monkeys.

Blood smears from three normal human beings were carefully examined and although the search for these organisms was diligently made, none was found. Smears were made from the bloods of thirteen normal monkeys with negative results. After inoculation with the virus these same monkeys gave positive results. The blood of other normal monkeys gave negative results.

Blood smears were stained with iodin and sulphuric acid in order to test the organisms for cellulose, but no blue stained organisms were seen.

Smears from the cords and brains of paralyzed monkeys, and from one human case were examined, but none of the new organisms was found.

Filtered virus stained with carbol-thionin and by Gram's method showed none of these organisms.

Defibrinated blood, three weeks to two months old, from two paralyzed monkeys, showed the forms in increased numbers.

Cultures made from the blood of a paralyzed monkey, in blood bouillon, plain bouillon, and blood-agar, examined after having been inoculated three weeks, showed the presence of the organism in increased numbers. Dorsett's egg medium was inoculated with the same blood at the same time but the organism was not found in smears from the surface of the medium or from the water of condensation.

SUBSEQUENT FINDINGS

Since publishing the above preliminary report on the finding of rod-shaped microorganisms in specimens of stained blood taken from human beings suffering from poliomyelitis and from monkeys in which the disease had been produced experimentally, these microorganisms have been found moving freely in the serum or attached to the side of a red blood-corpuscle in fresh blood taken from three monkeys ill of poliomyelitis. The monkey blood was examined at the time of inoculation and at twenty-four-hour periods up to 168 hours after inoculation. In the blood examined at the time of inoculation and at the twenty-four-hour period no organisms were found. At the end of forty-eight hours, however, a few of the moving microorganisms were found. Their numbers in the fresh blood specimens were increased up to 120 hours, after which time they seemed to appear in about the same numbers till examination at regular intervals was discontinued. At the end of three weeks the motile organisms could still be found in large numbers in the fresh blood.

Examination of the blood of a normal monkey examined at the same period as a control, failed to reveal any of the microorganisms.

The motility was of a slow, sinuous type resembling that of a spirillum. The bulbous ends were readily discernible. At times the organism appeared as standing on end, presenting the bulb uppermost, so that it resembled a large coccus in the microscopic field. Presently it would right itself and the long curved rod terminating in this bulb could be distinctly followed.

Pure cultures of this organism were isolated from the bloods of these three monkeys, on a medium made of the central nervous system of a monkey, combined with agar-agar. After a generation or two on this central-nervous-system-agar, the organism grows well on the ordinary laboratory media.

CHARACTERS OF THE ORGANISM

The morphologic, biologic and biochemic characters of the organism grown on artificial media are as follows:

The best stain to bring out the morphology is carbol-thionin, though Loeffler's alkaline methylene-blue, Giemsa, Wright's, Ziehl-Nielson, carbol-fuchsin and Gram's method demonstrate the organism with no difficulty whatsoever. Stained with carbol-thionin the organism appears as a granulated rod, the young forms measuring 0.6 to 0.8 microns in width by 1 to 2 microns in length. The older forms may appear as long as 10 or 12 microns with a width of 0.6 to 0.8 microns. Many of the indeterminate forms appear as spirals with from two to four loose turns. The longer forms have in many instances bulbous ends which have somewhat the appearance of spores, though free spores have never been observed.

The organism is actively motile, having a single polar flagellum at one pole only. It has no demonstrable capsule, and it is decolorized by the method of Gram. Colonies on agar are circular, moist, convex, entire, 1 to 3 mm. in diameter. In color they are bluish gray by direct light, old colonies having a yellowish tinge by transmitted light. Their peripheries are translucent while their centers are thickened and appear yellowish-white. Microscopically they are brownish-white, with a finely granular translucent periphery, and an opaque, brown, grumous center.

Agar Slant: Bluish gray with a suggestion of greenish tinge in cultures three or four days old, moist, raised, regular edges, growth along whole length of streak. White beaded growth in stab.

Gelatin: White, beaded growth along needle track with nail-head, moist growth on surface. No liquefaction.

Potato: Moist, cream to brown, abundant.

Central-Nervous-System-Agar: Gray, moist, very abundant along entire path of inoculation.

Egg Medium (consisting of yolk only): Moist, very abundant, spreading, pinkish growth.

Bouillon: Very turbid, white flocculent sediment. In 120 hours a white ring around the glass tube at the level of the surface of the medium.

Litmus Milk: An initial acidity followed by a gradually increasing alkalinity, with a beginning reduction of the litmus at the bottom of the tube. No coagulation of the casein occurs. In four weeks acidification again takes place; reduction of litmus and firm coagulation after five weeks.

There is a slight production of acid in dextrose-agar and saccharose-agar, but not in mannite, maltose or lactose. Gas production does not occur in any of the sugars above mentioned. Mannite turns green after three weeks. The organism grows best in neutral medium, next best in acid, and poorest in alkaline.

Indol is not produced. It seems to grow most abundantly on media rich in phosphates. It does not grow well on media containing much glycerin. The organism grows in the absence of air as well as when the air is given free access.

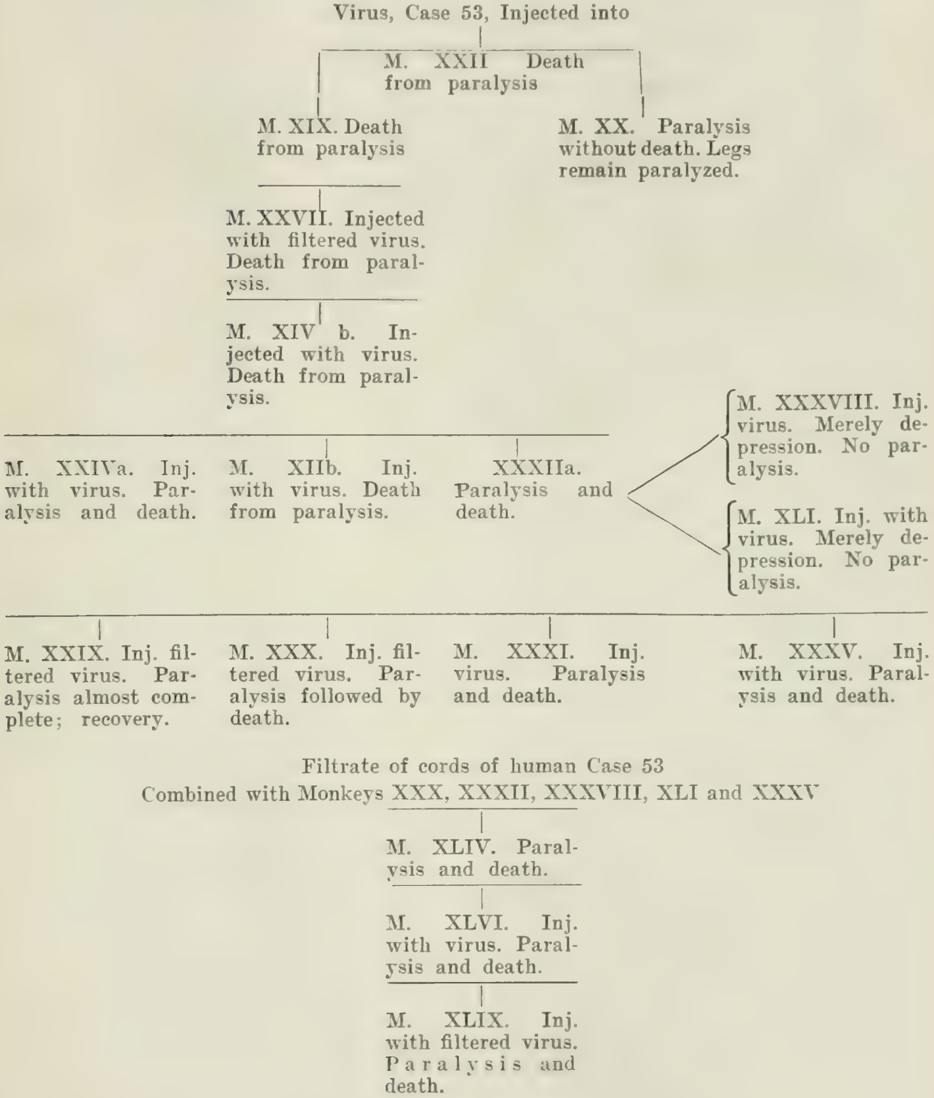
EXPERIMENTAL PRODUCTION AND PREVENTION OF THE DISEASE

Experiments on the production of poliomyelitis in monkeys by using this organism are in progress.

We have published in connection with our laboratory work negative experiments resulting from a good many observations made with great care. On finding virus negative after an autopsy had been performed on a child dead with this disease, we conducted experiments to determine what agent in the embalming fluid might have been destructive, and.

determining that formaldehyd and arsenic were both used in these fluids, a series of experiments were carried out with each, as well as with the fluid itself, solutions being injected at varying intervals as inoculation experiments to determine whether or not it would be possible to prevent the development of the disease by administration of these chemicals. The results in each instance were negative. Salvarsan was tried in a

Table 5.—Showing Transmissibility from Human Case to Monkey and from Monkey to Monkey



Virus, Case 53, Injected into

M. XXII Death from paralysis

M. XIX. Death from paralysis

M. XX. Paralysis without death. Legs remain paralyzed.

M. XXVII. Injected with filtered virus. Death from paralysis.

M. XIV b. Injected with virus. Death from paralysis.

M. XXIVa. Inj. with virus. Paralysis and death.

M. XIIb. Inj. with virus. Death from paralysis.

XXXIIa. Paralysis and death.

M. XXXVIII. Inj. virus. Merely depression. No paralysis.

M. XLI. Inj. with virus. Merely depression. No paralysis.

M. XXIX. Inj. filtered virus. Paralysis almost complete; recovery.

M. XXX. Inj. filtered virus. Paralysis followed by death.

M. XXXI. Inj. virus. Paralysis and death.

M. XXXV. Inj. with virus. Paralysis and death.

Filtrate of cords of human Case 53
Combined with Monkeys XXX, XXXII, XXXVIII, XLI and XXXV

M. XLIV. Paralysis and death.

M. XLVI. Inj. with virus. Paralysis and death.

M. XLIX. Inj. with filtered virus. Paralysis and death.

series of experiments in order that we might have data concerning the most potent arsenical preparation. These experiments, too, were negative, although they led to the incidental discovery of a positive Wassermann reaction in a monkey.

Abstract Case No. 256 (Laboratory Case No. 53).—G. T., female, aged 7; physician, Dr. George E. Day, Strasburg. Child well to August 23; August 24, stiffness of knee, pain in neck, fever, constipation, dizziness, temperature 102.5 F., no paralysis; August 26, paralysis right leg, both arms, loss of reflex, sensation normal; August 27, worse, pulse rapid, pressure symptoms; lumbar puncture secured 32 c.c. spinal fluid under excess pressure; August 28, slight improvement; 29th, breathing labored, 30th, death 9:00 a. m.; complete autopsy 11:00 a. m. Abundant material for laboratory study was obtained and true pathologic picture found. Tissues gave Noguchi butyric reaction. Emulsion from lumbar cord, bulb, pons, lymph-nodes, cultures from cerebrum, cerebellum, pons, bulb, lumbar cord, lymph-nodes; Gram positive coccus found in cultures taken at autopsy from brain and cord; nothing further by dark-field illumination. Monkeys inoculated with this coccus remained well. Two monkeys received emulsion from cord, pons and bulb into brain; both contracted disease and from this strain of virus successful transmission experiments were secured as illustrated on protocol of transmissibility.

I am greatly indebted to Dr. B. Franklin Royer, Chief Medical Inspector, and the staff of the Division of Medical Inspection, for the compilation of the statistics in this report, and to Drs. Herbert Fox, and J. B. Rucker, Jr., of the Laboratory Division, for the notes of the experimental work carried out under my direction.

RELATIONSHIP OF GASTRIC TO PANCREATIC FAT DIGESTION IN INFANTS *

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MINNEAPOLIS

The presence of a ferment in the adult stomach, which has the power of splitting neutral fat into its component fatty acids and glycerin, the gastric lipase, has been confirmed by recent studies.

Although Marcet,[1] Cash,[2] Ogata[3] and Vaughan Harley[4] found fatty acids in the stomach contents, it remained for Volhard[5] to demonstrate the presence of fat-splitting ferment and bring the subject forward for study. Stade,[6] one of Volhard's pupils, confirmed his results and suggested the technic of examination which goes by his name.

Inouye[7] failed to find evidence of a gastric lipase, but Falloise[8] confirmed its presence, and Laquer found the secretion from a Pawlow small stomach to be active in splitting fat, thus proving that the activity cannot be due to regurgitated pancreatic steapsin. Stef. v. Pesthy[8] confirmed the fact that fat is split in the stomach.

The study of the gastric lipase in the infant was first taken up in 1905 and its presence demonstrated by one of us (Sedgwick)[10] and the results published in 1906. This work showed that there is a fat-splitting ferment present in the infant's stomach, and in the glycerin extract of the gastric mucous membrane. It was demonstrated that lipase is present during the first few hours of life in the rabbit, and at least as early as on the fourteenth day in the infant. The fat was found to

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*Read in the Section on Diseases of Children of the American Medical Association, at the sixty-second annual session, held at Los Angeles, June, 1911.

*From the Laboratory of Physiological Chemistry, University of Minnesota.

1. Marcet: Med. Times and Gaz., New Series, 1858, xvii.

2. Cash: Ueber den Anteil des Magens und des Pankreas an der Verdauung der Fette, Arch. f. Anat. u. Physiol., 1880, 323.—Cited from v. Noorden's Handbuch der Pathologie des Stoffwechsels, i, 37.

3. Ogata: Die Zerlegung neutraler Fette in lebendigen Magen, Arch. f. Anat. u. Physiol., 1881, vi, 515; cited from Jahrb. d. Fortschr. d. Thierchemie, 1882, xi, 290.

4. Harley, Vaughan: Brit. Med. Jour., 1897, i, 1218.

5. Volhard: München. med. Wchnschr., 1900, 5 and 6.

6. Stade: Untersuchungen über das fettspaltende Ferment des Magens, 1902. Braunschweig, Vieweg and Son.

7. Inouye: Archiv. f. Verdauungskrankheiten, ix, 326.

8. Falloise, A.: Arch. internat. de physiol. iii, 396-497.

9. Pesthy, Stefan v.: Arch. f. Verdauungskr., xii, 292; cited from Jahresb. u. d. Fortschr. d. Tierchemie (Maly), xxxvi, 363.

10. Sedgwick: Jahrb. f. Kinderh., lxiv, 194; Arch. Pediat., 1906, xxiii, 414.

be split to the extent of from 2.9 to 10.6 per cent. in the recovered gastric contents; and *in vitro,* using egg yolk emulsion according to Stade, it was found that as high as 24 per cent. of the fat was split in twenty-four hours. The acids recovered were mostly higher members of the series, insoluble in water and not volatile.

This work on the infants was very shortly confirmed by Heinsheimer.[11] Rietschel[12] did not find any fat-splitting power in the gastric juice from the Pawlow stomach of 8-day-old suckling pigs. Rietschel, however, expressly states that, because of the difficulty in collecting a sufficient working quantity from such small animals, the juice with which he worked was kept some hours or even days under toluol in the ice chest.

Ibrahim[13] found lipase to be absent in fetuses of 150 gm., 250 gm. and 780 gm., but present in small quantities in a fetus of 800 gm., and plainly present in those from 1,100 gm. upwards. The fat-splitting power was very strong in the glycerin extract of the gastric mucosa of a 9-months-old infant which died of pneumonia. Ibrahim's statement regarding the toluol is as follows:

> "How can our positive results be brought into line with the negative findings of Rietschel and Engel? We believe it is the toluol that is to blame for the discrepancy. I know perfectly well that Sedgwick and Heinsheimer worked with toluol and got positive results. I suspect that they used but small quantities of toluol. We have been able to show, in a special series of experiments, that the toluol has a markedly inhibitory or completely suspending effect on the activity of lipase from the infant's stomach. It appears to act by an effect on the egg emulsion, for the juice which is freed from the excess of toluol by filter paper possesses fermentive activity. We used thymol. The addition of 2 per cent. sodium fluorid seems also not to be disturbing. We found later also that Laquer has noted this effect of toluol on the gastric lipase. I believe therefore that negative results which are gained in the presence of toluol should be considered of little importance."

This has been quoted in full to correct a mistake, and to call attention to an observation published by Sedgwick in 1906, which has not come to Heinsheimer's attention. The statement in Sedgwick's article,[10] that all his experiments were conducted under toluol, is an error which crept in after the manuscript left his hands, as such was not the case. In fact in the *Archives of Pediatrics*[10] the full data of an experiment showing the inhibitory action of toluol are given. Hecht[14] was able also to confirm the presence of a gastric lipase as well as the high per cent. of higher fatty acids which result from its action. The presence of lipase in the gastric juice of infants may therefore be considered to be established.

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[11] Heinsheimer: Deutsch. med. Wchnschr., xxxii, 1194.

[12] Rietschel: Monatschr. f. Kinderh., vi, 333.

[13] Ibrahim: Verhandl. d. deutsch. Gesellsch. f. Kinderh., Koln, 1908, p. 36.

[14] Hecht: Wien. klin. Wchnschr., 1909, 1404.

The presence of steapsin in the pancreatic juice of adults is so well known as to require no further discussion. Pancreatic steapsin has also been found in the infant.

As the gastric lipase acts on emulsified fat (Volhard), and as the food of the infant contains fat in an emulsified state only, the study of the fat ferment becomes of especial importance for the first year of life. It has been stated above that the fat-splitting in the stomach is limited in quantity. Considering these facts we began the study of the relationship between the gastric and pancreatic fat digestion.

In order to obtain gastric lipase entirely free from pancreatic steapsin we used the secretin from a Pawlow small stomach of a dog.[15] This was active, as the following results show:

Egg emulsion, 10 c.c., + thymol in chloroform were left in the incubator at 37 C. for twenty-four hours; 100 c.c. of ether were then added and the whole thoroughly shaken. After standing, 50 c.c. of the supernatant fluid were poured off and after the addition of phenolphthalein, required 1.2 c.c. n/10 NaOH for neutralization. A parallel experiment with the addition of 3 c.c. of the gastric juice from the Pawlow small stomach required 4.5 c.c. n/10 NaOH.

This shows a definite splitting.

In connection with the Schütz-Borissow law that the product of digestion is as the square root of the quantity of ferment, the following is of interest, as indicating that the splitting is due to a ferment. Treated as above:

One c.c. of Pawlow gastric juice split off 2.4 n/10, 4 c.c. of Pawlow gastric juice split off 4.9 n/10, almost exactly twice the amount, or $\sqrt{4}$.

Nine c.c. however required but 3 c.c., which may mean that the acidity became so high as to inhibit the action.

The technic of Donath[16] was then used, modified as follows:

Twenty c.c. of neutralized olive oil emulsion were held at 37 C. under varying conditions, as indicated in Table 1, and titrated at the end of stated intervals with n/10 NaOH.

As the experiments recorded in Table 1 show, the attempt was made to subject the emulsion in flask *b* to conditions similar to those in the body—that is, two hours under the influence of gastric juice, then neutralized and digested with pancreatic extract for three hours. The fatty acids produced required 66.1 c.c. n/10 as compared with 53.7 c.c. n/10 required in experiment *c,* which was not acted on preliminarily by the gastric juice. The amount of fat split was 23 per cent. greater when the emulsion was subjected to the gastric lipase before the pancreatic ferment. Control experiment *a,* in which neither ferment was used,

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[15] We are indebted to Dr. A. E. Wilcox for the skilful operation on the dog.

[16] Donath, H.: Aktivierung u. Reaktivierung von Pankreassteapsin, Beitr. z. chem. Physiol. u. Path., 1907, x, 390.

TABLE 1.—EXPERIMENTS TO SHOW THE RELATIONSHIP BETWEEN GASTRIC AND PANCREATIC FAT DIGESTION

20 c.c. of emulsion+

	a	*b*	*c*	*d*
Water	7 c.c.	0	2 c.c.	5 c.c.
Gastric juice from stomach of dog	0	2 c.c. 2 hrs. Neutralized	0 2 hrs.	2 c.c.
Pancreatic extract*	0 5 hrs.	5 c.c. 3 hrs.	5 c.c. 3 hrs.	0 2 hrs.
n/10 NaOH	9 c.c.	66.1 c.c.	53.7 c.c.	1.5 c.c.

20 c.c. of oil emulsion+

*The pancreatic extract was composed of commercial pancreatin and glycerin.

TABLE 2.—EFFECT OF BOILED GASTRIC JUICE ON COMBINED FAT-SPLITTING ACTION

Egg yolk emulsion, 10 c.c.

	a	*b*
Water	3 c.c.	3 c.c.
Juice from small stomach*	2 c.c. 2 hrs. Contents neutralized at end of 2 hrs.	2 c.c. 2 hrs. Neutralized after 2 hrs.
Pancreatic extract	5 c.c. 3 hrs.	5 c.c. 3 hrs.
Titration n/10 NaOH	17.7 c.c.	20.1 c.c.

*Gastric Juice Boiled in *a* but not in *b*.

TABLE 3.—EXPERIMENT IN FAT-SPLITTING USING EGG YOLK EMULSION

Egg yolk emulsion 10 c.c.

	a	*b*
Juice from small stomach	5 c.c. 2 hrs.	5 c.c. 2 hrs.
Water	0 Neutralized at end of 2 hrs.	5 c.c. Neutralized
Pancreatic extract	5 c.c. 3 hrs.	0 3 hrs.
First titration: 100 c.c. of ether added to each, *a* and *b*, shaken and settled: supernatant fatty acid solution, 50 c.c. + 75 c.c. of alcohol requires for neutralization, n/10 NaOH.	7.3 c.c.	3.0 c.c.
Second titration of fatty acids from fat not split by the ferment	16.3 c.c.	20.0 c.c.
	23.6 c.c.	23.0 c.c.

TABLE 4.—EXPERIMENTS WITH EGG YOLK EMULSION, USING GASTRIC CONTENTS FROM AN INFANT

10 c.c. egg yolk emulsion+

	a	*b*	*c*
Gastric contents from an infant	5 c.c. In the incubator 2 hrs.; alkalinized*	5 c.c. As *a*	0
Pancreatic extract	0 3 hrs. longer at 37 C.	5 c.c. As *a*	5 c.c.
100 c.c., ether added and titrated and as in Table 3—			
First titration n/10 NaOH	2.2 c.c.	6.8 c.c.	3.8 c.c.
Second titration n/10 NaOH (after saponification)	35.0 c.c.	30.2 c.c.	
	37.2 c.c.	37.0 c.c.	

*Neutralized + 2 c.c. NaOH.

could be neutralized by 0.9 c.c. n/10 NaOH. This shows the extent of the splitting due to the ferments. Control *d*, in which the gastric juice alone was used, shows that the inferior and slow action of the gastric lipase alone cannot account for the extent of the splitting.

In Table 2 it is shown that when the digestion is carried on with boiled gastric juice for two hours before the pancreatic extract is added the combined splitting action is lessened.

The two experiments tabulated in Table 3 were carried out as follows:

Egg yolk emulsion was used containing three yolks to 100 c.c. in both. To 10 c.c. of this fat emulsion, flask *a*, 5 c.c. of juice from the small stomach of the dog were added and kept in the incubator with thymol and chloroform for two hours. At the end of this time the digestion was neutralized and 5 c.c. of pancreatic extract were added. Flask *b* was treated in the same manner, with the gastric juice, but the pancreatic extract was omitted. Both flasks were again placed in the incubator for three hours, at the end of which time 100 c.c. of ether were added to each, and both were shaken and allowed to settle. Fifty c.c. of the supernatant fatty acid solution obtained were added to 75 c.c. of alcohol and titrated. Contents *a*, which had been subjected consecutively to both ferments, required 7.3 c.c. n/10 NaOH. Contents *b*, which had been acted on by the gastric ferment alone, required but 3 c.c., less than half as much.

The experiments in Table 4 were carried on as in Table 3, using gastric contents from an infant instead of the gastric juice from the small stomach of the dog. The egg emulsion digested with 5 c.c. of gastric contents for two hours, neutralized, and then rendered alkaline by the addition of 2 c.c. n/10 NaOH, and digested further for three hours, after being treated with ether and alcohol as before, gave a titration of 2.2 c.c. n/10.

When the pancreatic extract was added after the two-hour digestion with gastric ferment the titration was 6.8 c.c. n/10. When digested three hours with the pancreatic juice alone the titration was 3.8 n/10.

Gastric digestion alone five hours	2.2
Pancreatic digestion alone three hours	3.8
	6.0
Gastric digestion two hours alkalinized + pancreatic digestion three hours	6.8

From the above we feel warranted in concluding that the neutralization of the fat gastric digestion does not end the function of the gastric lipase of the dog or infant. Whether the effect shown is a summation of, or a relationship between, the actions of the two ferments, preparatory or activating, our results do not permit us to state with certainty. It seems justifiable, however, to conclude that the function of the gastric lipase of the infant is not ended when the gastric contents pass the pylorus and are neutralized in the duodenum.

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HIPPURIC ACID IN THE URINE OF NORMAL BREAST-FED INFANTS *

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The urine of the normal breast-fed infant is mainly distinguished by negative characteristics. This is a statement made by Mayerhofer[1] in his recent paper. In this paper attention is called to the absence of such substances as glycuronic acid, indican, urobilin, etc., in the urine of these individuals. According to the same author some of the products normally encountered in the urine of adults, like the substances paired with glycocoll, namely, benzoic acid, etc., have not been made the subject of detailed investigation. With regard to the occurrence of hippuric acid in the urine of infants, only a few scanty references came to our notice. Marchand[2] as well as Meissner and Shephard[3] state that the occurrence of hippuric acid in the infant's urine is a well-known fact. Amberg and Morrill,[4] examining 260 c.c. of a mixed urine obtained from several healthy breast-fed infants, were unable to demonstrate the presence of free or combined benzoic acid. From the examination of this amount of urine of such low cencentration no definite conclusions could be drawn. It was therefore thought advisable to repeat the examination with a larger amount of urine. Thanks to the kindness of Dr. Williams of the Obstetrical Department, we were able to collect about 1,900 c.c. of urine from normal breast-fed infants. The amount obtained from the different babies was as follows:

Infant	Collection started, days after birth	Urine Collected, days	Amount collected, c.c.
1	10	2	409
2	6	6	426
3	6	6	914
4	23	2	162
			1,911

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*From the Department of Pediatrics and the Department of Pharmacology, Johns Hopkins University.

1. Mayerhofer: Chemische Teilerscheinungen im Harne gesunder und kranker Säuglinge, Ztschr. f. Kinderh., 1911, i, 487.

2. Marchant: Ueber die Oxydationsproducte des Leims, etc., Jour. f. pract. Chem., 1845, xxxv, 309.

3. Meissner and Shephard: Untersuchungen über das Entstehen der Hippursäure; Hanover, 1866.

4. Amberg and Morrill: Ein Stoffwechselversuch, etc., Jahrb. f. Kinderh., 1909, lxix, 280.

The babies had surpassed their birth weight when the urine was collected and were in perfect condition clinically. To exclude the possibility of slight digestive disturbances 10 c.c. of each sample of urine was used for the determination of phosphoric acid. Moll[5] has shown that the amount of phosphoric acid excreted in the urine of breast-fed infants may serve to indicate very slight digestive disturbances. Only such urine was used as corresponded to the standard established by Moll for the urines of the class "free from phosphates." Therefore we have reason to assume that the urine examined by us was obtained from perfectly healthy individuals.

The method of analysis employed is that of Jaarsveld and Stokvis,[6] which was retested by Van de Velde and Stokvis.[7]

It is not our purpose to discuss here the literature concerning the occurrence of hippuric acid in the urine of animal and man under different conditions, nor the various methods for its determination. References to the literature may be found in the report of the United States Department of Agriculture.[8]

Each portion of urine was immediately evaporated to a small volume with the addition of some sodium carbonate, transferred to a flask and preserved with toluol until the total amount was collected. The method of analysis may be described briefly. The urine evaporated to a small volume is acidified with hydrochloric acid and thoroughly extracted with acetic ether after standing twenty-four hours. The acetic ether extract is washed with water and evaporated at room temperature, the residue containing free and combined benzoic acid, if any is present. The free benzoic acid is extracted with petrol ether. The residue is hydrolyzed by boiling with strong sodium hydroxid, thus liberating the benzoic acid from hippuric acid. After cooling, the fluid is acidified with hydrochloric acid and after standing over night, thoroughly extracted with petrol ether. This extract is evaporated at room temperature, leaving the benzoic acid.

Examined by this method, the urine did not show any crystals on evaporation of the acetic ether extract, nor was any benzoic acid found after the hydrolysis of the residue from this extract. There was no evidence of the presence of either free or combined benzoic acid. As with other methods of hippuric acid determination in urine, small amounts may escape detection. We may mention the statement of Wiechowski[9]

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5. Moll: Die klinische Bedeutung, etc., Jahrb. f. Kinderh., 1909, lxix, 129.

6. Jaarsveld and Stokvis: Ueber den Einfluss der Nierenaffectionen, etc., Arch. f. exper. Path. u. Pharm., 1879, x, 268.

7. Van de Velde and Stokvis: Experimentelle Beiträge, etc., Arch. f. exper. Path. u. Pharm., 1883, xvii, 189.

8. The Influence of Sodium Benzoate on the Nutrition and Health of Men, Bull. 88, U. S. Dept. Agriculture, 1909.

9. Wiechowski: Die Gesetze der Hippursäuresynthese, Beitr. z. chem. Physiol. u. Path., 1906, vii, 204.

that the method of Jaarsveld and Stokvis gives good results even in the presence of small amounts of hippuric acid.

Since the question of the presence or absence of hippuric acid in the urine of the normal breast-fed infant is of considerable interest, it would have been desirable to extend our investigations with the employment of different methods of analysis, but we were unable to obtain the necessary amount of urine. Nevertheless, from the result just recorded it does not seem probable that a very appreciable part of the nitrogen contained in the urine of the normal breast-fed infant is excreted in the form of hippuric acid.

The character of the food—mother's milk, with its content of lactalbumin—is such that it could supply sufficient glycocoll for the formation of hippuric acid. But even if the food should not yield glycocoll on decomposition, this substance could be furnished by the animal organism. For instance, Grosser,[10] feeding young goats with casein and giving benzoic acid, found hippuric acid in the urine. Furthermore, Brugsch and Hirsch,[11] as well as Feigin,[12] found hippuric acid in the urine of hunger artists. To demonstrate that the normal breast-fed infant can readily furnish glycocoll, such a baby received 0.5 gm. of sodium benzoate. During the next twenty-four hours 175 c.c. of urine were collected, yielding, on evaporation of the acetic ether extract, hippuric acid.

The absence of demonstrable amounts of hippuric acid from the urine of the normal breast-fed infant depends, therefore, on the absence of benzoic acid. Most authors agree that the benzoic acid normally entering into the production of hippuric acid in man is either derived from benzoic acid or related substances contained in food, or from putrefactive processes in the intestinal canal.[13] Since it is known that putrefactive processes are, as a rule, in abeyance in the intestinal canal of perfectly normal breast-fed infants, the absence of hippuric acid from the urine would not be surprising. Quite recently Simon,[14] using the method of Henriques and Soerensen,[15] claims to have demonstrated the presence of hippuric acid in the urine of the breast-fed infant. In this method the hippuric acid is also extracted with acetic ether. The residue is decomposed with hydrocholoric acid and the nitrogen of the resulting glycocoll is determined by means of the formol titration. In the first three days after birth the hippuric acid excretion was found to be rather high, running later on a lower level. The lowest figure was found on the eighth day (case Brunner), when 225 c.c. of urine yielded 0.005 gm. of nitrogen, corresponding to 0.0639 gm. of hippuric acid. The urine of our infants was collected later than the third day after birth; that is, when the excretion of hippuric acid has reached a lower level. If we calculate the amount of hippuric acid that should be present in the 1,911 c.c. of urine, using the lowest figure given by Simon, we should have 0.543 gm. of hippuric acid, or 0.37 gm. of benzoic acid. It is very unlikely that the urine examined by us should have contained an amount of hippuric acid approaching such a figure.

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[10] Grosser: Beitrag zur Bewertung des Albumingehalts, etc., Jahrb. f. Kinderh., 1911, lxxiii, 103.

[11] Brugsch and Hirsch: Gesammt N, etc., Ztschr. f. exper. Pathol. u. Therap., 1906, iii, 638.

[12] Feigin: Ueber die Hippursäurenscheidung, etc., Inaugural dissertation, Berlin, 1906.

[13] See, for instance, Baumann: Die aromatischen Verbindungen, etc., Ztschr. f. physiol. Chem., 1886, x, 123; Gerhardt: Ueber Darmfäulniss, Ergebn. d. Physiol., 1904, iii, 138.

[14] Simon: Zur Stickstoffverteilung im Urin des Neugeborenen, Ztschr. f. Kinderh., 1911, ii, 1.

[15] Henriques and Soerensen: Ueber die quantitative Bestimmung, etc., Ztsch. f. physiol. Chem., 1909, lxiii, 27.

FURTHER OBSERVATIONS OF THE ACID CONTROL OF THE PYLORUS IN INFANTS *

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In a former paper[1] we recorded two experiments on the acid control of the pylorus in infants. We have since extended and verified these results and present them herewith, together with a partial description of the first experiments.

HISTORICAL NOTE

The explanation of the opening and closing of the pylorus was not fully made until Pawlow and Cannon's work was done. Not long after Beaumont's experiments in 1832 it is true that Hirsch, by means of a duodenal fistula in a dog, came to the conclusion that acid on the duodenal side caused the pylorus to close, but he abandoned his idea in favor of von Mering's observations, made about the same time, that the closure of the pylorus was due to the bulk of liquid or food in the duodenum. In his experiments von Mering introduces milk into the duodenum. The observation that the mechanical effect of inflating a small rubber balloon in the duodenum causes the pylorus to contract and its rhythmic movements to cease, seemed to lend support to von Mering's theory.

It was left for Pawlow and Cannon, however, to clear up these discrepancies and make full explanation of the phenomena observed by Hirsch and von Mering. Pawlow demonstrated that milk or neutral fat in the duodenum, whether in small or large bulk, excites the duodenal closing reflex and keeps the pylorus closed until the neutral fat has become saponified or until it has passed on into a lower segment of the intestine. He also showed that acid on the duodenal side closed the pylorus. Later Cannon demonstrated that acid in the stomach opens the pylorus and that the differential escape of carbohydrates and proteins from the stomach is due to their respective stimulating and combining property for hydrochloric acid. Hence the observations of Hirsch and von Mering were correct, but their explanations were entirely faulty.

AUTHORS' EXPERIMENTS

The experiments which resulted in the above observations were performed on dogs and cats. Of the various methods used Cannon's is

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*From the Pediatric Clinic, University of Michigan.

*Read at the Meeting of the American Pediatric Society, Lake Mohonk, May, 1911.

[1] Arch Pediat., February, 1911.

probably ideal, as it removed practically all abnormal conditions. In conducting our experiments we have been aware of the arguments against the accuracy of the method of tubing the stomach and we have not lost sight of the possible effect of the preantral sphincter on our results. The small size and the elasticity of the infant's stomach better adapt it for such observations than the adult stomach, and for these reasons we believe that the method we used, properly controlled, fully demonstrates the point at issue.

Method.—We selected babies who had proved their indifference to the passage of the tube. That is, they had become accustomed to the tube and retained it with perfect ease for any period desired. They would often sleep throughout an experiment, excepting for the brief interval of passing the tube. We found No. 14 (English) soft rubber catheter connected by a piece of glass tubing with a rubber tube and small bulb the most satisfactory apparatus for our work. As we had not investigated the effect of posture on the rate of stomach evacuation we had the position of the infant constant; that is, lying on the left side.

Control Test Meal.—Skim-milk, diluted one-half with water, was employed as a suitable test meal for these investigations. The meal usually contained a fraction of 1 per cent. of fat and proved more convenient to work with than milk containing a higher fat per cent., and this removed from discussion the possible effect of fat on the pyloric reflex. A definite amount was delivered to the stomach through a tube and allowed to remain a definite time. It was then recovered by expression and syphonage as described below.

Acid Meal.—This meal was prepared by treating skim-milk with dilute hydrochloric acid (10 per cent. solution) until the acidity desired was obtained. The food was then kept at body temperature for an hour to insure complete combination of the acid with the protein. It was then retested and treated, if necessary, to insure the acid value as it entered the stomach.

Basic Meal.—The basic calcium casein meal was prepared by adding the requisite amount of lime water to the skim-milk to render it faintly but distinctly alkaline to phenophthalein. The balance of the dilution was then made up with water so that, as with the control and acid meal, the skim-milk formed half of the mixture. This meal was also retested to insure its alkalinity as it entered the stomach.

Calculation of Error.—It could not be expected that work of this kind would be trustworthy for comparisons, excepting in marked differences. To ascertain what our error would be in infants who had not been previously tubed or selected for investigation because of their particular adaptability, we made sixteen observations on infants taken at random. These are recorded in Table 1. In most of these cases the infants were allowed to go three and a half hours after a feeding before giving the test-water. If the stomach was empty we introduced 45 c.c. of plain water through the catheter, recovering it immediately by expression and syphonage. In each case the water was completely delivered to the stomach, none being allowed to remain in the tube. The syphonage was started by expression, one of us pressing over the epigastrium. It will be seen that our greatest error in recovering the contents is 5 c.c. and that the error is seldom greater than 3 c.c. In most instances a little mucus was recovered, As stated before, the infants with which this investigation had to do were carefully selected and caution was observed to wash and drain the stomach. In these babies our error[1] was less than 3 c.c.

TABLE 1.—SIXTEEN INVESTIGATIONS ON INFANTS TAKEN AT RANDOM TO DETERMINE ROUGHLY THE ERROR IN RECOVERING IMMEDIATELY BY MEANS OF STOMACH TUBE, A GIVEN AMOUNT OF FLUID DELIVERED TO THE STOMACH BY GAVAGE

No.	Name	Interval Since Last Feeding hours	Condition of Stomach	Amount of water Given, c.c.	Amount of water Recovered, c.c.	Condition of water Recovered
1	Edwards	3½	Empty	45	40	About ½ c.c. mucus
2	Hessler	3½	Empty	45	45½	....
3	Rush	3½	Empty	45	46	A little mucus
4	Kinyon	2½	Empty	45	46	Tinged yellow
5	Wilcox	3½	Empty	45	41	....
6	Rush	3½	2 c.c.	45	43	Few fine curds
7	Mills	3½	Empty	45	40	A little mucus
8	Hessler	3½	Empty	45	45½	Plugs of mucus
9	Simmons	3½	Empty	45	46	Considerable mucus
10	Hackford	3½	Empty	45	49	2 or 3 c.c. mucus
11	Hacket	3½	Empty	45	44	½ c.c. thick mucus
12	Rush	3½	Empty	45	41	Few fine curds
13	Hatzke	3½	Empty	45	40	Little thick mucus
14	Mills	3½	Empty	45	44	Few fine curds
15	Nering	3½	Empty	45	45	A little mucus
16	Hessler	3½	Empty	45	41	A little mucus

SERIES I.—THE EFFECT OF ACID ON THE DUODENAL SIDE OF THE PYLORUS

The three sets of experiments recorded in Charts 1, 2 and 3 have to do with the duodenal side of the pyloric reflex. The control meals enter the stomach, remain there for a certain time, until the acid reflex on the stomach side causes the pylorus to open. The acid meal enters the stomach with immediate stimulus for the pyloric opening reflex. As soon as it reaches the duodenum, in proportion to the amount ejected and its acidity, the pylorus remains closed. As our acid meal causes the pylorus to remain closed a comparatively long time, we speak of this as a sustained duodenal reflex, in contradistinction to the normal pyloric reflex and the delayed pyloric reflex recorded in our second series.

CASES 1 AND 2.—The data relating to these infants will be found in our previous report.[1] Both were in good health and gaining in weight. At no time

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2. Greatest error in any one case 5 c.c. Average error 2.38 c.c.

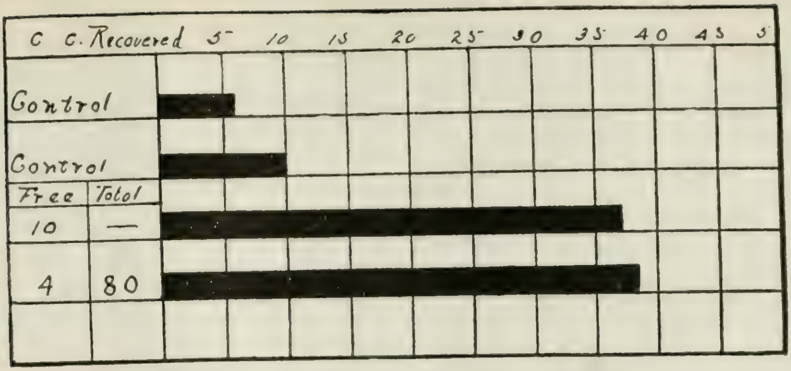

Chart 1.—Sustained duodenal reflex, Case 1.

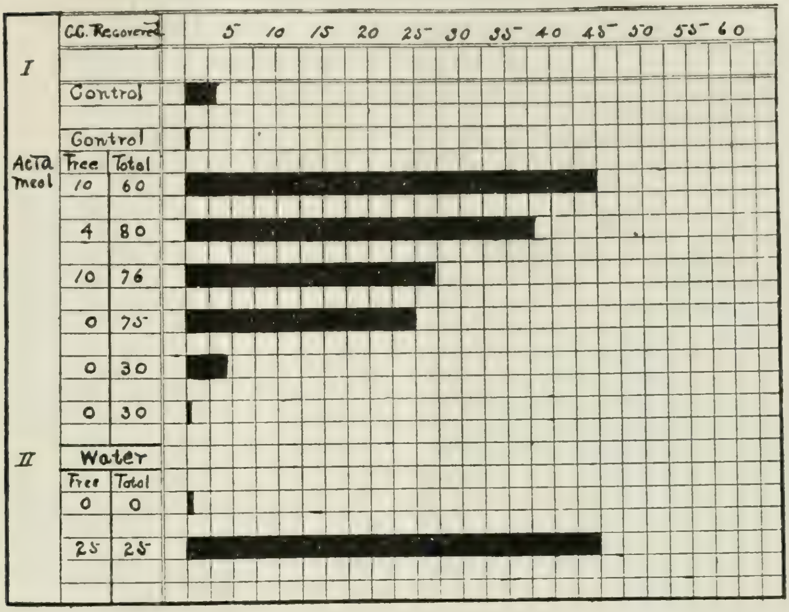

Chart 2.—Sustained duodenal reflex, Case 2. The secretion of this infant's stomach was always normal. There was no free HCl.

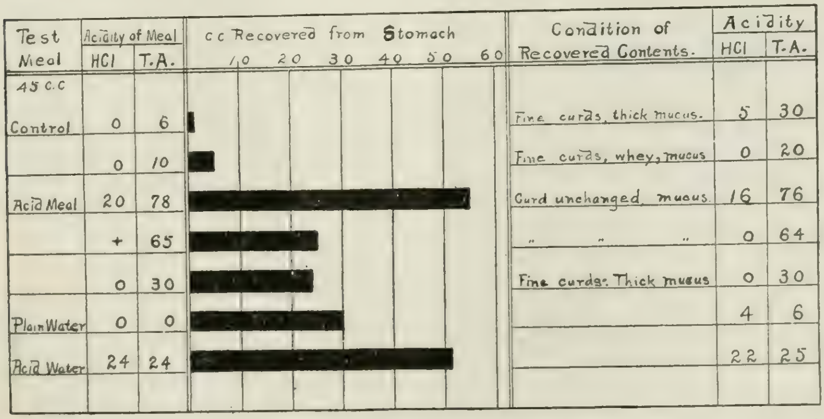

Chart 3.—Sustained duodenal reflex, Case 3. The secretion of this infant's stomach was always hypernormal. Free acid occurred in the fasting stomach.

in either case were we able to find any free hydrochloric acid. The delayed evacuation of the stomach is well shown in the acid meals. The higher the acidity, or the more acid present, the larger the amount recovered at the end of the period. This is particularly well shown in Case 2.

Case 3.—A well developed baby. History and physical examination negative. On referring to the series of stomach analyses (Table 2) it will be seen that the infant almost always secreted acid to the free point and at times gave a free acid value as high as 25 and 35, a true hyperchlorhydria for an infant. In addition to this, there were evidences of hypersecretion during the period of our observations. How long such a condition would continue without producing spasm, if it ever would, we cannot say, as the infant soon passed from under our observation.

There was nothing in Case 3 to suggest ulcer, either peptic or duodenal. We find in this case, three hours after an ordinary feeding, when the stomach is practically free from food remains, a free acid value of 5. We also find that plain water leaves this baby's stomach much more slowly than does the control milk meal and the water meal in Case 2. It is believed, and supported by experiment, that water leaves the stomach almost directly. The reason for this, however, has never been satisfactorily explained. In this case we think the delayed evacuation of water can be explained by the presence of free acid in the fasting stomach and the hypersecretion. The water does not take up the acid but, known, may provoke a further secretion in this neurosis, hence duodenal reflex is sustained longer than under normal conditions. In Case 2 we had no such condition to contend with. Free acid was never detected and the total acidity after an ordinary or test meal was never high, accordingly there was little or no neutralization to take place in the duodenum and the water passed on uninterruptedly into the gut.

Table 2.—Results of Experimental Feeding in Case 3, Showing Hypersecretion and Hyperchlorhydria*

Meal	Time in Stomach, Hours	Amount Fed, c.c.	Amount Recovered, c.c.	Free HCl ...	Total Acid ....
2-6-¾-W.	?	90	0	—	—
½ S. M. and water ..	¾	90	2	5	30
2-6-¾ W.	2	90	5	25	60
½ S.M. and water ..	¾	90	5	0	20
2-6-½-W.	2¾	90	4	35	70
2-6-½-W.	2½	90	7	35	70
Plain Water	¾	90	30	4	6
2-6-½-W.	?	90	2.5	15	60

*Abbreviations: 2-6-¾=2% fat, 6% sugar, ¾% protein. W=whey made up the balance of the mixture. ½ S.M.=Half skim milk and water.

DETAILED ACCOUNT OF EXPERIMENTS

Control Meal No. 1. Infant 36 Days Old. May 11, 1910

8:50 a. m. Three hours and fifty minutes after 90 c.c. 2-6-¾-whey mixture; nothing obtained through tube; stomach washed with 90 c.c. water; all recovered, containing about 1 per cent. fine curds and mucus.

8:55 a. m. Fed 90 c.c. half skim-milk and water, through a No. 14 catheter; total acidity of food; fat .9 per cent.

9:40 a. m. (45 minutes) 2 c.c. whey; mucus thick; a few very fine curds recovered; stomach washed with 85 c.c. water; 83 c.c. containing about 2 per cent. thick mucus and a few small curds recovered. Free HCl 5; total acid 30.

Control Meal No. 2. Infant 37 Days Old. May 12, 1910

8:40 a. m. Two hours and forty minutes after 90 c.c. of 2-6-¾ whey mixture; 5 c.c. recovered, containing 50 per cent. curds, and mucus thick. HCl 25; total acid 60. Stomach washed with 40 c.c. warm water; 40 c.c. recovered practically clear.

8:45 a. m. Five minutes later, fed by gavage 90 c.c. half skim-milk and water; total acid 10; fat .8 per cent.

9:30 a. m. (45 minutes) 5 c.c. recovered; whey containing a few small curds and mucus. HCl 0; total acid 20.

Acid Meal No. 1. Infant 38 Days Old. May 13, 1910

6:00 a. m. 90 c.c. 2-6-½ whey nursed.

8:45 a. m. 4 c.c. recovered, containing 25 per cent. thick mucus and a few small curds, HCl 35; total acid 70. Stomach washed with 45 c.c. warm water; all recovered, containing 2 per cent. thick mucus.

9:00 a. m. Fed 90 c.c., half skim-milk and water acidified by gavage. Free HCl 20; total acid 78.

[illegible] a. m. (45 minutes) 55 c.c. milky material recovered containing 20 per cent. very fine curds and thick mucus. The whey is very milky. HCl 16; total acid 76. Stomach washed with 45 c.c. warm water; all recovered; slightly opaque with milky material.

Acid Meal No. 2. Infant 42 Days Old. May 16, 1910

9:45 a. m. 90 c.c. half skim-milk and water, acidified, fed. Free HCl trace; total acid 65.

10:30 a. m. (45 minutes) 25 c.c. recovered. Same condition as when it entered stomach, excepting a little mucus. HCl 0; total acid 64. Stomach washed with 80 c.c. water; 82 c.c. recovered; slightly turbid.

Acid Water Meal Experiment. Infant 42 Days Old. May 16, 1910

6:00 a. m. 90 c.c. 2-6-½ whey nursed.

8:30 a. m. 7 c.c. recovered containing 50 per cent. thick mucus and curds. HCl 35; total acid 70. Stomach washed with 45 c.c. warm water; 46 c.c. recovered, slightly cloudy.

8:40 a. m. Fed 90 c.c. plain water by gavage.

9:10 a. m. 30 c.c. recovered containing a little thick mucus. HCl 4; total acid 6.

9:13 a. m. Fed 90 c.c. acidified water, HCl 24, by gavage.

9:43 a. m. (30 minutes) 51 c.c. recovered. Free HCl 22; total acid 25.

Acid Milk Meal No. 3. Infant 43 Days Old. May 17, 1910

8:55 a. m. 2.5 c.c. containing 60 per cent. thick mucus and curds recovered from stomach. Free HCl 15; total acid 60. Stomach washed with 95 c.c. warm water; 90 c.c. recovered containing 2 per cent. fine curds and mucus.

9:00 a. m. 90 c.c. half skim-milk and water, total acidity 30, given by gavage.

9:45 a. m. (45 minutes) 24 c.c. clear whey containing a few small curds and considerable thick mucus recovered. HCl 0; total acid 30. Stomach washed with 45 c.c. warm water; all recovered practically clear.

SERIES II.—THE EFFECT OF ACID ON THE STOMACH SIDE OF THE PYLORUS

In this series the control meal enters the stomach under the same conditions as before; there is a food stimulus for the secretion of acid to open the pylorus, while in the basic or alkaline meal, although the food stimulus, so far as we know, is exerted on the secretory mechanism of the stomach, the presence of alkali to the point of saturation of the protein delays the acid in reaching the point for stimulation of the opening reflex; hence at the end of forty-five minutes a very much larger amount is recovered than in the control experiments—not 5 or 10 c.c., but double and treble the amount.

It will be observed in these experiments that at times we recovered as much as 15 c.c. more, at the end of the period, than we had put in. This was at a time preceding the opening reflex and represents roughly the amount of gastric juice secreted. In Case 4 we recovered at the end of thirty minutes 15 c.c. more than we put in; at the end of forty-five minutes we recovered a few c.c. more than we originally put in, but about 12 c.c. less than we reintroduced into the stomach. In this experiment, if we had again introduced the contents removed at forty-five minutes, ten minutes later we might have experienced what we have on more than one occasion—the stomach almost empty. The pyloric reflex has just begun to operate and because of the low acidity of the food either a large gush or a series of rapid short gushes has evacuated the stomach. On one occasion at forty-five minutes nearly all the food was present in the stomach, and no curd formation had taken place; in fifty minutes only a small amount of curded material could be recovered.

These experiments, we think, give abundant proof that the pylorus is governed by acid on both sides of the pyloric ring and confirm, in man, the experiments in animals done by Pawlow, Cannon and others.

Case 4 (Charts 4 and 5).—Baby G., an apparently normal infant. History and physical examination negative. On referring to the series of stomach analyses, Table 3, it will be seen that this infant never secreted free acid and that the total acid was never excessively high.

Table 3.—Results in Free HCl and Total Acidity in Feeding Experiments in Case 4

Meal	Time in Stomach, Hours	Amount Fed, c.c.	Amount Recovered c.c.	Free HCl	Total Acidity ......
2-6-½	1¾	75	27	0	32
½ S.M. and Water	¾	45	13?	0	26
2-6-½ W.	2¾	45	26	0	32
½ S.M. and Water	5/6	45	?	0	15
2-6-½ W.	½	30	30	0	44
2-6-½ W.	2¾	90	1	0	—
½ S.M. and Water	⅔	45	?	0	12
2-6-½ W	...	..	..	.	..

DETAILED ACCOUNT OF EXPERIMENTS IN CASE 4

Control Meal No. 1. Infant 30 Days Old. May 25, 1910

7:30 a. m. Nursed 75 c.c. 2-6 ½ mixture.

9:13 a. m. 27 c.c. recovered, containing 15 per cent. curds and thick mucus. HCl 0; total acid 32. Stomach washed with 90 c.c. water; 90 c.c. recovered, containing 2 per cent. curds.

9:20 a. m. 45 c.c. half skim-milk and water, total acidity 10, given by gavage.

9:50 a. m. (30 minutes) 13 c.c. of fluid were expressed, consisting of whey, medium sized curds, and thick mucus. This was returned to the stomach.

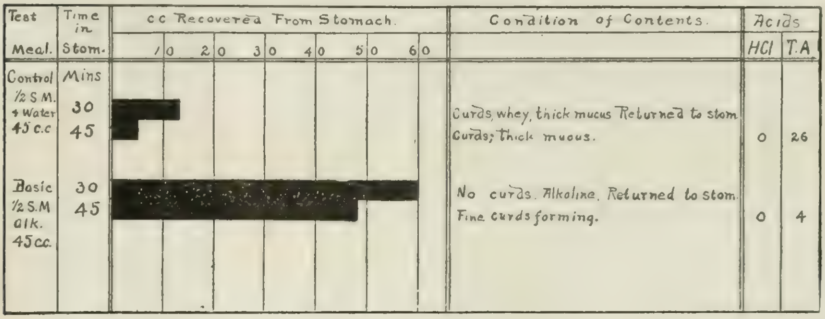

Chart 4.—Delayed pyloric reflex. Case 4, Experiment 1, showing the effect of alkali on stomach evacuation. The secretion of this infant's stomach was always normal.

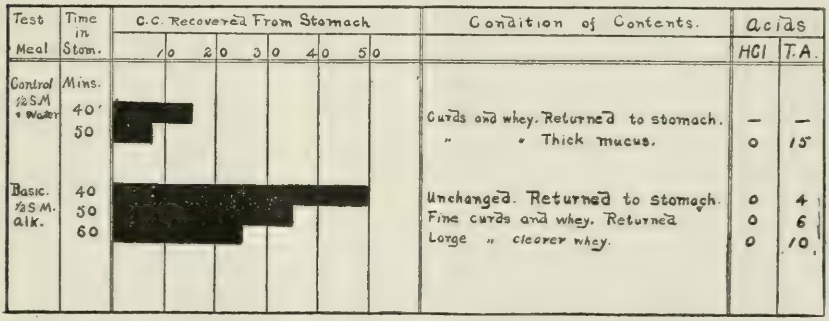

Chart 5.—Delayed pyloric reflex. Case 4, Experiment 2, showing the effect of alkaline contents on stomach evacuation.

10:05 a. m. (45 minutes) 15 c.c. of fluid were expressed consisting of 20 per cent. large curds and some thick mucus. HCl 0; total acid 26. Stomach washed with 90 c.c. water; 88 c.c. returned practically clear.

Basic Meal No. 1. Infant 30 Days Old. May 25, 1910

10:10 a. m. 45 c.c. of half skim-milk and water, rendered basic with lime water, were given by gavage.

10:40 a. m. (30 minutes) 60 c.c. recovered; no curds; reaction alkaline to litmus; returned to stomach.

10:55 a. m. (45 minutes) 49 c.c. Fine curds beginning to form. HCl 0; total acid 4. Stomach washed; only a few fine curds returned.

Remark: It will be observed that thirty minutes after feeding we recovered 15 c.c. more than was introduced, and that no curd formation was present; that fifteen minutes later curds had formed and 45 c.c. were recovered. No stimulus to pyloric opening was present until about this time. The 15 c.c. doubtless represents grossly the amount of gastric juice secreted during the first thirty minutes' stay in the stomach. See Chart 4.

Control Meal No. 2. Infant 32 Days Old. May 27, 1910

6:00 a. m. Fed 45 c.c. 2-6-½ whey mixture.
8:40 a. m. 26 c.c. recovered; 30 per cent. curds and thick mucus. HCl 0; total acid 32. Stomach washed with 90 c.c. warm water; all recovered, containing a little over 1 per cent. fine curds and mucus.
8:45 a. m. 45 c.c. half skim-milk and water, total acid 9, given by gavage.
9:25 a. m. (40 minutes) 15 c.c. expressed, consisting of fine curds and whey. Returned to stomach.
9:35 a. m. (50 minutes) 8 c.c. fluid containing 20 per cent. medium small curds and a little thick mucus recovered. HCl 0; total acid 15. Stomach washed with 90 c.c. water; 89 c.c. recovered, containing a few fine curds and mucus hardly measurable by centrifuge.

Basic Meal No. 2. Infant 32 Days Old. May 27, 1910

9:40 a. m. 45 c.c. one-half skim-milk and water, rendered basic with lime water, were given by gavage.
10:20 a. m. (40 minutes later) 50 c.c. recovered; no distinct curds; appears about the same as when introduced. Total acid 4; returned to stomach.
10:30 a. m. (50 minutes) 35 c.c. recovered; distinct fine curds and whey. Free acid 0; total acid 6. Returned to stomach.
10:40 a. m. (60 minutes) 25 c.c. recovered; curds larger and more separated from the whey. HCl 0; total acid 10. Stomach washed clear.

Basic Meal No. 3. Infant 36 Days Old. May 31, 1910

5:00 a. m. 75 c.c. 2-6-½ whey mixture.
8:00 a. m. 15 c.c. 2-6-½ whey mixture.
8:30 a. m. 30 c.c. of whey containing 2 per cent. curds and a little thick mucus recovered. HCl 0; total acid 44. Stomach washed with 130 c.c. warm water. All recovered plus a little mucus.
8:55 a. m. 45 c.c. one-half skim-milk and water, rendered basic, given by gavage.
9:35 a. m. (40 minutes) 35 c.c. recovered, containing 20 per cent. curds, whey and thick mucus. Tube was repeatedly blocked by the curds. HCl 0; total acid 8. Stomach washed with 90 c.c. warm water; 90 c.c. recovered, containing a few small curds and considerable thick mucus.

Control Meal No. 3. Infant 38 Days Old. June 2, 1910

6:00 a. m. 90 c.c. 2-6-½ whey mixture.
8:45 a. m. 1 c.c. thick mucus recovered. HCl 0. Stomach washed with 45 c.c. warm water; all recovered, perfectly clear excepting a little mucus.
8:55 a. m. 45 c.c. plain one-half skim-milk and water were given by gavage; total acidity 8.
9:15 a. m. (20 minutes) 45 c.c. recovered; fine curds beginning to form. Returned to stomach.
9:25 a. m. (40 minutes) 30 c.c. recovered; curds more distinct; mucus more marked. Returned to stomach.
9:35 a. m. (50 minutes) 15 c.c. recovered, whey containing 5 per cent. large curds; tube blocked with thick mucus. HCl 0; total acid 12. Stomach washed clean.

It may be asked what practical bearing these observations have on gastro-enterologic therapy and on our knowledge of gastro-enteric diseases. It was Dr. Cowie's object in starting these observations to see if the management of pyloric stenosis in infants, both true and false, could be put on a scientific basis. Most cases of this character have been treated without reference to the pyloric reflex or the altered physiologic conditions present. We believe there is a certain group of cases in which these are important factors to determine. It would seem at least possible to recognize varying degrees of stenosis and readily to differentiate them from what may be called pseudo-stenosis or spasm and to enable us to observe the effect of the reaction of the food given on the duration of the duodenal closing reflex, which seems to be an important factor in many cases. This will be considered in a later article.

CONCLUSIONS

1. The pyloric opening and closing reflex can be easily demonstrated in infants' stomachs.
2. In experimental acid stomach contents the duodenal closing reflex is sustained and consequently the evacuation of the stomach is delayed.
3. In experimental alkaline stomach contents the pyloric opening reflex is delayed and consequently the evacuation of the stomach is delayed.
4. Free acid is not necessary for pyloric opening. Its presence has a tendency to provoke prolonged duodenal closing in an infant.
5. In hypersecretion in infants protein-containing food appears to leave the stomach more readily than water because of its binding property for acid.

Lawrence Building.

THE RELATION OF MEAT INGESTION TO INDICANURIA IN CHILDREN *

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With the view of gathering, if possible, some data on the use and abuse of meat diet in childhood, the work reported in this paper was begun about a year ago. It was hoped that the results of the experiments might lead to some definite indications as to the quantity and frequency with which this article of diet should be allowed.

So much work has been done on the dietetic requirements of infancy, and from both theoretical and practical standpoints so many valuable conclusions have been drawn, that it seems strange that more work has not been done to settle the same problems in older children.

The insidious, often marked, symptoms that chronic dietetic disturbances show after two years of age, compared with the more acute signs of intestinal indigestion in infancy, probably account for the rather neglectful attitude that even pediatrists have taken toward regulating the diets of older children.

If one makes it a practice to discuss with his patients their attitude towards the giving of meat to children, he will find as a rule that one of two rather disagreeable conditions exists. Either the child receives no meat at all, the parents laboring under the only too frequently met delusion that meat soups contain all of the valuable constituents of the food, or that the child receives meat twice or even three times a day. It is a question which of these two evils is the worse. The one that puts on the kidneys the duty of excreting a wealth of useless extractives, or the one which forces on the youthful organism three meals a day—more than sufficient to supply the caloric needs of a working adult. One thing is definite, however, and that is that if the next generation of men and women is to be a healthy one we must so regulate the conditions under which the children live that their growth may not be impeded by chronic intestinal disturbances.

During the past two years a large number of stools has been examined incidental to routine investigation, and while it has been strikingly common to find free starch and free fat, especially in those children with clinical symptoms of intestinal disturbance, it has been rather sur-

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*Read in the Section on Diseases of Children at the Sixty-Second Annual Session of the American Medical Association, held at Los Angeles, June, 1911.

prisingly rare to find undigested muscle-fiber, except in the most marked cases. Bearing this in mind, and desiring, if possible, to reach some conclusion as to the advisability of giving meat to children over two years of age, it was decided to investigate the pathologic products which the urine might contain, which might have some bearing on this subject.

Taking into consideration that an excess of meat in the diet would probably lead to improper digestion and consequent putrefaction, it seemed reasonable to assume that the amount of indican in the urine of children fed on small and large quantities of meat might throw some light on the subject.

Appreciating the fact that under normal circumstances little or no indican is excreted in the urine, it seemed possible that if meat were given in excess, digestion would be sufficiently interfered with to allow the putrefactive bacteria to act on the excess of protein, and the indicanuria would be a gauge as to the ability of the organism to properly handle the animal food.

It is almost universally conceded now, as Nencki and others have shown, that indol, the forerunner of indican, is produced in the intestine solely by bacterial putrefactive decomposition of the protein food. There have been a few dissenters from this view, notably, Flint, who states that it may be formed by the action of the tryptic ferment of the pancreatic juice on the protein food. Herter states that such a phenomenon could only occur in the intestines in the presence of excessive amounts of protein food combined with greatly delayed digestion. Ordinary absorption occurs in the peptone and amino-acid stage of proteolytic digestion and it is hardly conceivable that a rapidly proteolyzed meal should lead to the formation of indol. In unmistakable and most conclusive support of the bacterial putrefactive source of indol, stands the work of Senator, who in a large number of investigations failed to detect the merest trace of indican in the urine of new-born babies, the stools of which are always bacteria-free.

The object in selecting indican as the urinary by-product, which might throw some light on the use of meat diet in childhood, was twofold. First, because it has been definitely proved that one of the chief causes of indicanuria is an excess of food, which by hampering digestion allows the putrefactive bacteria to work, and second, because it seemed advisable, if possible, to have some single test that might be of use to the ordinary practitioner.

That accurate nitrogen and sulphur determinations may in the future throw some light on this very interesting subject is probable, but this does not come within the province of anyone but the trained chemist and is therefore of little value in aiding the clinician.

The minute details of a well-planned piece of investigation which one can carry out successfully in a properly organized laboratory, are not within the power of the best intentioned worker when he has to deal with institutional children as the objects of his experiments; and when, furthermore, he has to depend on the gracious willingness of institutional attendants to carry out instructions as to diets, he is truly in a dilemma that is discouraging. On account of this difficulty, which is practically unsurmountable, it seemed advisable to pursue the work without disturbing the routine of the home from which the specimens were obtained, knowing that quantitative diets could not be given, and that only untrained assistants would have to be depended on to furnish the daily specimens of urine. The diets given to the children corresponded to the diets usually given to children in the ordinary orphanages and no attempt was made to modify this under the first series of tests that was carried out.

A brief résumé of this diet may be *apropos* in order that one may understand fully the most important factor in determining the conclusions. For breakfast: fruit, cereal, toast and milk. Dinner: milk soup, meat, potatoes, green vegetable, and dessert. Supper: bread, milk and fruit. The diets were somewhat variable as to the particular kinds of cereals, meats and vegetables, but otherwise were fairly constant.

With the object in mind of determining the influence which age had on the ability to digest meat, it was decided to divide the children into four groups. In the first group were six children 12 years of age. In the second group, six children 9 years of age. In the third group, six children 6 years of age, and in the fourth group, six children 3 years of age. The early morning urine was the sample tested in each case and the Obermayer test was the one employed in formulating the results.

A rather arbitrary method was used for designating the quantity of indican present in each specimen, + representing a moderate reaction, + + a marked reaction, and + + + a very marked reaction. The children on whom the tests were made were normal children as far as physical examination could determine. In each case the urine was carefully examined in order to exclude pathologic conditions of the kidney, and no child was observed in whom the urine showed the slightest deviation from the normal.

In the first group of children tested were six normal girls, 12 years of age, in each of whom twenty-five specimens of urine were examined, making a total of 150 experiments, in fifteen of which on different days a single + reaction was obtained. In other words, 10 per cent. of the specimens of urine of 12-year-old institutional children showed a moderate reaction for indican, indicating a slight amount of intestinal putrefaction with the diet which they were receiving.

In the second group of children were six girls 9 years of age. One hundred and fifty specimens of urine were tested and twenty of them showed a single + reaction with the routine diet, a slight increase (13 per cent. as compared to 10 per cent.) over the number of positive reactions among the 12-year-old children but not sufficient to warrant any deduction.

In the third group of children were six girls 6 years of age. One hundred and fifty specimens of urine were examined and in about 15 per cent. of the examinations a single + reaction was obtained.

In the fourth group were six children 3 years of age, and the results here were decidedly interesting because they showed that in children of this age the amount of protein food received in an ordinary diet containing milk and meat once daily gave rise to considerable intestinal putrefaction and indicanuria. Twenty per cent. of these examinations showed a moderate single + reaction and 15 per cent. gave a marked + + reaction. In all of the cases under observation, one or more normal bowel movements occurred every day, so that constipation could in no way have had an influence on the results.

These experiments, which were made with the children receiving ordinary diets, were now repeated after the children had been given meat twice daily for two weeks. The instructions given were that the children under observation should receive the same diets as previously, except that they should receive in the evening the same quantity of meat as at noon. In the 150 tests made on the urine of the 12-year-old girls, 2 per cent. showed a marked double + + reaction and 12 per cent. showed a moderate single + reaction. The results were practically identical with those obtained when the children were getting meat but once daily. In the 150 tests made in the second group of children 9 years of age, 14 per cent. showed a moderate single + reaction, these results also being practically the same as when the children were getting meat only once daily.

In the observations made on the 6-year-old children who were receiving meat twice daily, the results were rather more striking. Twenty-five per cent. showed a moderate single + reaction for indican and 15 per cent. showed a marked double + + reaction. This was a decided increase in the number of positive reactions—25 per cent. of moderate single + reactions as compared with 15 per cent. and 10 per cent. of marked double + + reactions as compared with no + + reactions when the children were receiving meat but once daily.

In the 3-year-old children the results were also very striking. Thirty-five per cent. of the reactions were single + or moderate reactions and 30 per cent. were double + + or marked reactions as compared with

20 per cent. of moderate reactions and 15 per cent. of marked reactions in these same children when they were receiving meat but once a day.

The results, while strongly suggestive, and while warranting one in advocating certain principles in the feeding of children, might be criticized on the ground that the conclusions are not based on the observation of a sufficiently large number of children. Admitting this, still the absolutely negative results in the 9- and 12-year-old children, with the positive results in the 3- and 6-year-old children are very suggestive.

A brief résumé of the results obtained shows as follows:

1. With an ordinary diet containing meat once daily, children 6, 9 and 12 years old succeed in digesting their food fairly well without much putrefaction in the intestinal tract. Three-year-old children, on the other hand, with the same diet are much more apt to show indicanuria.

2. The giving of meat twice daily produces in 9- and 12-year-old children practically no change in the amount of intestinal putrefaction.

3. In 6- and even more markedly in 3-year-old children meat given twice daily gives rise to a decided increase in the indicanuria and is a cause of pronounced intestinal putrefaction.

4. As limited as these observations may be, they seem to point to one definite conclusion, and that is that the giving of meat more than once daily to children under 9 years of age is a practice conducive to intestinal putrefaction and indicanuria, and is to be deprecated on account of the harm resulting to the organism from the constant presence of abnormal products of putrefaction.

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THE TREATMENT OF CHRONIC NEPHRITIS IN CHILDREN BY THE EDEBOHLS OPERATION *

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The treatment of chronic forms of nephritis by an operative procedure of splitting the capsule of the kidney was first proposed by Edebohls and advocated by him as a mode of curing ultimately the disease of these organs and restoring them to normal condition, that is, of curing the nephritis. In his list of seventy or more cases of nephritis he reports seventeen patients as permanently cured; that is, casts and albumin had disappeared from the urine, and the patients were fully restored.[1] However this may be, I have not undertaken the treatment of the cases which form the basis of this paper with any such purpose in view. It can scarcely be conceived that an organ so irreparably damaged as those of any of my patients could be restored to its original integrity. The object for which I submitted the patients referred to in this paper to operation was less ambitious and still humane. In children no disease subjects the victim to more suffering than chronic incurable disease of the kidney. The general anasarca alone makes a species of bedridden sufferer of the little one, and anything or any operation which would eliminate this one symptom and enable the patients to take their place among the apparently well would and must receive more than passing notice. It should be remembered that of the five cases here recorded all of the patients were chronic invalids, four for very long periods of time; some of the patients had been repeatedly in the hospital to be treated for recrudescences of symptoms. All of the patients for a length of time extending over months had been subjected to other forms of treatment, having in view a relief of the distressing symptoms of anasarca and uremia, and all these forms of treatment had failed, not on account of any lack of persistence in treatment, but because it was impossible to make the crippled organ respond to any known forms of medical management.

Under these conditions and in face of the fact that the patients were chronic bedridden invalids, the Edebohls operation was performed simply in the hope of relieving the anasarca and restoring the patients to an

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* Read before the Association of American Physicians, May, 1911.

[1] There was only one case in Edebohls' series of a child who was operated on. Whether this is the same child reported by A. Caillé in the Transactions of the American Pediatric Society, Vol. xiv, I cannot say. The number of cases in the literature of children suffering from nephritis who have been operated on by the Edebohls operation and subsequently studied are exceedingly few.

existence at least simulating health. This was attained in four of the five patients operated on. In three cases the return after the severe operation to a condition of ambulatory well-being was gratifying; one patient was lost sight of after being in excellent condition fully a year, and the fifth died as a direct result of the failure of the operation to cause a response on the part of the kidneys. In no case could it be said that the operation endangered life. Drs. Lilienthal and Elsberg were the surgeons who readily supported the idea of subjecting the patients to this operation at my suggestion. The operation is in itself well borne by the patient and the recovery from the so-called shock and anesthetic is very prompt indeed.

REPORT OF CASES

Case 1.—H. R., male, aged 11, was admitted October 15, 1905.

Family History.—Father, mother and two other children alive; no history of renal disease in the family.

Previous History.—Measles at 3 years; scarlet fever at 4 years. Three months after the scarlet fever the patient had swelling of the face for a few days, which disappeared spontaneously; had headache about every two weeks since his attack of scarlet fever. At these times he felt nauseated, usually vomited and then felt better. There was no history of rheumatism, malaria, typhoid, ear disease or jaundice; no cardiac history.

Present Illness.—This began two months ago; mother first noticed swelling of the boy's face. He had suffered no unusual exposure. A few days later swelling of the abdomen was noticed and again in a few days edema of the feet became prominent. At first there were no subjective symptoms. Later the child complained of slight dyspnea; occasionally there was vomiting and abdominal pain. These symptoms continued until admission. For the previous eight days the vomiting had been severe, the patient vomiting almost everything he ate; had been constipated for a week and had passed very little urine. There was no change noticed in the amount of urine he passed until one week previous to admission. Appetite was poor; had no spots before the eyes; headache had not troubled him recently.

Physical Examination.—General condition good; well nourished.

Skin: Pale, slight puffiness of cheeks and lower eyelids.

Eyes: Pupils negative; scleræ very white.

Mouth and Throat: Teeth and gums in fair condition; tongue moist and slightly coated; throat, negative.

Glands: Considerable glandular enlargement in axillary regions; moderate enlargment in posterior cervical, submaxillary, epitrochlear and inguinal regions.

Lungs: Anteriorly and posteriorly over both chests were heard sibilant sounds with expiration. From the angle of the scapula to base, both sides posteriorly exhibited dulness, diminished fremitus and diminished breathing. Anteriorly there was a hyperresonant note over both chests.

Heart: Borders difficult to determine because of hyperresonance of chest; does not appear to be enlarged; apex beat not seen or felt; slight impurity of first sound at apex; moderate accentuation of both two-inch basic sounds, especially aortic; action regular, forcible, about normal in frequency; no murmurs.

Pulses: Equal, normal in force and frequency, rather large, regular; slight increase in tension.

Spleen: Not palpable.

Liver: Fourth space to sixth space to free border; not palpable.

Abdomen: Generally tympanitic; too tense for satisfactory palpation; not tender.

Lower Extremities: Knee-jerk markedly exaggerated; slight edema of legs.

Genitals: Negative.

Rectal: Negative.

October 27: The diagnosis was post-scarlatinal nephritis (large white kidney). There were pallor, puffiness of cheeks and lower-eyelids, signs of a moderate double hydrothorax, moderate soft edema of the legs and feet, accentuation of the second sound at both basic cardiac orifices, slightly increased pulse tension and considerable albumin, and hyaline and a few hyalo-granular casts in the urine. A fair amount of urine and urea was being excreted.

November 22: The various well recognized modes of treatment were found unavailing in this case. The anasarca persisted; no improvement in the renal condition as judged by the urine; there were still present pallor, puffiness of the cheeks, hydrothorax, ascites, considerable soft edema of the legs and feet, considerable albumin, casts and some red blood-cells in the urine; tongue moist and coated. Posteriorly on the left side of the chest, dulness began at the middle of the scapula, and became flatness, with fremitus and breathing at the base, diminished voice, breathing and fremitus over the dull area; similar signs though slightly less extensive on the right side. The heart, except for marked accentuation of second basic sounds, was negative. The left ventricle, however, seemed somewhat enlarged, the left border being outside the nipple line; abdomen gave signs of moderate amount of ascitic fluid; edema of penis and scrotum had increased.

November 23: *Operation.*—Decapsulation of kidneys for subacute nephritis by Dr. Lilienthal.

Right: Incision was made from just below border of ribs posteriorly, obliquely downward and forward toward ant-superior spine of ilium. On incising the subcutaneous tissue, a great amount of serous fluid exuded and the tissue appeared gelatinous. The muscular tissue appeared very pale and edematous. Incised between fibers of oblique muscles, and found that the incision was made entirely too high. Therefore, an incision was made through the skin downward and at right angles to first oblique incision. The muscles now retracted, the fatty capsule of kidney was incised and the kidney palpated high up under the ribs. With some difficulty the kidney was delivered into the wound. The capsule was incised along the posterior border and slipped easily from the kidney on each side to the pelvis of the kidney. The kidney was about twice the usual size. It was replaced and the muscles sutured with No. 2 chromic gut, by interrupted sutures in two layers. Drain to kidney and at lower angles; silk for skin.

Left: Oblique incision was made the same as above. Subcutaneous tissues and muscles presented same appearance as on right side. The fatty capsule was incised and kidney delivered into wound; it was found about one and one-half times its usual size. Capsule of kidney incised along posterior border and capsule stripped to pelvis on each side, but capsule seemed somewhat more adherent than on right side. Muscles sutured.

November 26: Following the operation patient passed about ℥xx of urine in twenty-four hours. The general condition was no worse than previous to the operation. The patient was comfortable, took his nourishment well, did not vomit, had no pain. The temperature had not been above 101 F., pulse of good quality. There was a profuse serous discharge from the wounds. On this date there was some increase in the edema; legs markedly edematous, ascites increased; signs of hydrothorax unchanged; considerable edema of scrotum and penis; acupuncture of scrotum and prepuce performed.

December 2: During the previous two weeks the ascites and anasarca were about the same as previous to the operation. Amount of urine passed in twenty-four hours was from ℥viii to ℥xiii. The discharge from the wounds, however, had a uriniforous odor, and probably considerable urine was excreted directly from the wound.

December 28: For the previous few days patient had been running a temperature (maximum 105 F.). He had been passing very small quantities of urine

(9-10ʒ during twenty-four hours). The edema of the face, abdomen, legs, penis and scrotum had increased. He complained of pain in the lumbar region and legs. There had been no headache or vomiting. The urine contained much albumin and a moderate amount of hyaline and granular casts.

January 1, 1906: Multiple puncture of penis and scrotum was done and wet dressing applied.

January 5: Since December 30 the patient's temperature had been normal. He had been passing fair amount of urine, which now contained only a trace of albumin, and a few hyaline and granular casts. The general condition was much improved. The anasarca was diminishing. There were no uremic symptoms. Patient was on soft diet.

January 19: The previous fourteen days the patient had been passing a small amount of urine. Puffiness of face and ascites had increased, but there was no increase in the edema of the legs. There had been no rise in temperature. The urine did not contain macroscopic blood, but only some red blood-cells. On this date the urine looked bloody and contained a great many blood cells, a great deal of albumin and hyaline and granular casts; also some pus and epithelial cells. Aside from the change in the character of the urine, the patient's condition had not changed. He was comfortable and had no vomiting, pains or cardiac palpitation, or any other uremic symptom.

January 27: There had been improvement in the patient's condition in the previous six days. He had been passing sufficient urine, which contained no macroscopic blood, but contained some albumin, hyaline, hyalogranular and granular casts and red blood-cells in moderate amount, about 2 gm. in twenty-four hours. Edema of face, ascites, edema of scrotum, prepuce and legs had disappeared entirely. There were no uremic symptoms.

February 22: Patient complained of sore throat and difficulty in swallowing. On inspection the throat was found to be reddened, the tonsils somewhat swollen, and there were a few enlarged and slightly tender lymph-nodes in the left submaxillary region. The temperature February 21 rose to 100.8 F. (it had not been above 100 for eleven days); February 22 it was 100.4 F. Aside from the angina, the patient was comfortable. The urine showed no change; it was alkaline, sp. gr. 1,028, contained albumin and a moderate number of hyalogranular casts, some red blood-cells and pus-cells.

March 9: General condition good; no edema; lungs negative; heart borders unchanged; second sound at base very slightly accentuated; pulse equal, good force, regular, no increase of tension. The urine showed a moderate number of very small hyaline casts, few pus-cells, and few red blood-cells.

March 24: Urine still contained pus, albumin and a moderate amount of hyalogranular casts; no red blood-cells. There was no edema, no dyspepsia, no tension. Discharged very much improved.

November, 1906: Patient continued in very good physical condition, without any edema or symptoms. A single fresh specimen of the urine was examined; it was alkaline, amber, and contained albumin, a moderate number of granular casts, epithelial cells, leukocytes and numerous red blood-cells.

April 28, 1906: The patient was in good condition; no symptoms; well nourished, rather pale, no evidences of cyanosis or dyspepsia; nothing suggestive of nephritis about facies. Heart showed some hypertrophy to the left of the apical impulse; strong second pulmonic accentuation; no edema; urine 1,020; contained casts and epithelial cells, but no red blood-cells; the number of formed elements was small in proportion to the albumin, which was large; pulse was regular, increased in tension.

May 26, 1906: Urine 1,026, acid, positive for albumin and contained hyaline, hyalogranular and granular casts, leukocytes and epithelium.

This case gives a history of a nephritis of at least seven years' standing, with a culmination of symptoms three months before ultimate operation, and a failure to respond to therapeutic measures which would enable the patient to be up and about. It should be noted that the improvement did not set in immediately, but was delayed, with even increased anasarca and diminution of urine for six weeks after the operation, when improvement set in and was progressive. The improvement was permanent and continued after operation, which, in view of the fact that this boy was not particularly well taken care of and was exposed to all kinds of weather, was certainly satisfactory.

CASE 2.—A. R., male, aged 6 years, was admitted in July, 1902.

Family History.—Negative.

Previous History.—No infectious diseases except scarlet fever three and one-half months prior to admission, which was complicated with nephritis; anasarca was general, urination diminished and the child had convulsions.

Present History.—This dates from this illness. Since the first acute attack the patient had never been well; had headache, diminished urination, swelling of abdomen, hematuria. These symptoms were present in varying severity at different times. For a week the patient had complained of anorexia and vomited for the first time; no convulsions since first attack; no fever; bowels constipated. Urination was scanty and contained blood. W. B. C. 14,000; blood smear negative.

Physical Examination.—General condition good; well nourished.

Glands: Large cervical, axillary and inguinal glands.

Lungs: Slight dulness at left base.

Heart: Right border at right border of sternum, upper border third rib. left border, nipple line. Action regular, sounds good, no murmurs.

Pulse: Regular, no increased tension, good quality.

Liver: Fifth space to free border; just palpable.

Spleen: Ninth rib to anterior axillary line; palpable one finger below costal border.

Abdomen: Lax; tympanitis; left kidney palpable; no general anasarca.

Extremities: Reflexes present; no clonus.

July 22: General condition good, lungs negative, heart borders normal, second sound at base, musical; spleen not palpable; left kidney still palpable.

July 26: Patient was running a slight temperature and passing plenty of urine.

July 30: Lung dulness, diminished voice and breathing at left base persistent. Abdomen slightly distended, some dulness in both flanks, note changing on change of position; urine contained faint trace of albumin, specific gravity low; temperature, respiration and pulse normal.

August 5: Albumin and casts reappeared in the urine.

August 10: General condition about the same. The patient was passing a large amount of urine; 50 ℥ August 9; .9 per cent. urea.

August 22: Passed fair amount of urine.

August 23: Discharged improved.

The temperature during the first three days was 98.8 to 101.6 F.; after that the temperature remained normal. Pulse and respiration were not accelerated. Urine on admission contained albumin, sp. gr. 1,014, acid, many hyaline granular and epithelial casts, red and white blood-cells; 2 per cent. urea.

At discharge the urine was acid, sp. gr. 1,012, contained albumin, a few pus-cells, red blood-cells and epithelial cells.

Treatment.—Tannic acid, Kemp's irrigations, fluid diet; later sodium iodid.

Readmitted, May 8, 1905: Since discharge the patient had been perfectly well; had not complained of headache; no edema of feet at night; no swelling of abdomen, no nausea or vomiting; passed normal amount of urine; no cardiac palpitation.

Present illness was of one and one-half weeks' duration. During this time the patient complained of headaches and pain in the abdomen; face, feet, legs and abdomen had been swollen and patient had been passing very small quantities of urine; no nausea or vomiting; no fever; bowels moved after cathartic; chief complaint, edema of face and ankles.

Physical Examination.—General condition good; marked puffiness of eyelids; skin and mucous membranes pale.

Lungs: Anteriorly, slight dulness at left apex and in lower part of both axillæ; diminished voice and breathing in lower part of both axillæ; posteriorly, dulness at left apex and on both sides from level of the angle of scapula, merging into flatness at base. Over upper part of dull areas voice and breathing were diminished, first at bases.

Heart: Borders as at last examination; apex beat not distinctly localized; impulse could be felt in fourth and fifth spaces in the nipple line; action slightly irregular; impurity of first sound at apex and accentuation of second sound; accentuated second aortic; no distinct murmurs.

Pulses: Equal, slow, slightly irregular, tension not increased.

Liver: Fourth space, sixth space to just below free border; palpable one finger below free border; not tender.

Spleen: Not felt.

Abdomen: Rounded, generally tympanitic, except for slight dulness in right flank, which does not change with change of position.

Extremities: Cyanosis of feet; marked edema of feet and legs.

May 12: Child was passing very small quantities of urine; edema of lids was more marked; also edema over bridge of nose; edema of legs about the same; well-marked edema of back.

May 14: Edema of face and legs had almost entirely disappeared; still slight edema of tissues of back, and slight dulness at bases.

May 20: Patient was up out of bed and as yet had no recurrence of the edema; difference in weight between when child was edematous and when edema had gone was 8 pounds.

May 29: Discharged improved.

Temperature on admission was 103.6 F. Next morning it was normal and remained so for the remainder of the child's stay at the hospital. Pulse 80 to 100.

Treatment.—Hot baths, salts in the morning; at times nitroglycerin and infusion of digitalis.

Urine on admission, reaction acid, sp. gr. 1,030, albumin positive; many hyaline and granular casts; few red blood-corpuscles and pus corpuscles; at discharge positive for albumin, sp. gr. 1,020, reaction acid; many hyaline casts, few pus corpuscles, bacteria, debris (24-hour specimen). Quantity varied from 9½ ℥ to 36 ℥ in twenty-four hours. The albumin varied from heavy trace to ++.

June 12, 1905, Readmitted.—After discharge for a few days the patient was kept quiet; after that he played rough games in the street. For a week he did not go to school and felt rather weak. Then he was sent to school for three days. For a week there had been edema of lower lids after sleeping. There had been dyspnea on climbing stairs for the last four days; swelling of the feet two or three days, face two days. Bowels moved three or four times a day until this date, when they moved only once. The urine had been steadily diminishing; passed only ℥ iv this date. The child was listless, had no appetite, complained of frontal headache. and the edema was more marked.

Physical Examination.—Edema of face, particularly of eyelids.

Lungs: Dulness with diminished voice and breathing at bases.

Heart: Borders normal; apex beat fourth space just within nipple line; action was arrhythmical, becoming rapid with inspiration and slow at expiration; sounds good; second aortic accentuated; no murmurs.

Pulses: Equal, same arrhythmia as heart; fair quality.

Liver: Fourth space, sixth space to free border; palpable two fingers below free border on deep inspiration.

Spleen: Not felt.

Abdomen: Rounded, rather tense, movable dulness in flanks; fluid wave not obtained; no tenderness; too tense for satisfactory palpation; circumference at level of umbilicus 64 cm.

Extremities: Well marked edema of feet and legs.

June 14: The edema, especially of face, is much more marked than on admission.

June 15: Dr. Lilienthal saw the patient June 14 and considered the case one likely to be benefited by an Edebohls operation.

June 17: Decided improvement in edema.

June 20: The improvement continued and the edema had now almost entirely disappeared; amount of urine in twenty-four hours had increased to over twice as much as on admission.

June 29: General condition about the same; still some puffiness under the eyes and slight edema of back and ankles. For the previous three days the patient had been passing less urine; the previous night had complained of headache. Pulses equal, regular, small, no increased tension. Temperature normal.

Operation.—June 30, decapsulation of kidneys for nephritis by Dr. Elsberg. A 2-inch curved lumbar incision was made and the kidneys exposed. They appeared large and red; capsules easily stripped off; capsules on both sides nonadherent, not tense, so that there was little retraction of the capsule when first incised. Almost the entire capsule on both sides was extirpated; small packing below each kidney; few No. 1 catgut sutures for muscles; silk for skin. Wound healed nicely.

July 1: Edema of back more marked; child passed small amount of urine; puffiness under eyes persisted; edema of lower extremities had increased since the previous night. There was slight edema of the scrotum; circumference of abdomen at level of umbilicus 64 cm.; second aortic sound slightly accentuated; slight increase of pulse tension.

July 6: Theobromin sodium salicylate (diuretin) was started July 5; child passed more urine.

July 7: Was passing small quantities of urine.

July 8: Edema of abdominal wall and flank. Circumference of abdomen at level of umbilicus 69 cm.

July 10: For last three days patient was passing more urine; edema still marked; breath was sweet, pulse good, no increased tension.

July 13: Was passing less urine again; edema less marked; was out of bed.

July 14: Edema of abdomen and scrotum was much less; circumference of abdomen 59 cm.

July 19: Movable dulness in left flank; no edema of scrotum; face was puffy; some edema of back and legs.

August 6: Patient was passing a fair amount of urine, but contains considerable albumin; general condition had improved, and patient was out of bed.

August 12: General condition fair; face was puffy in the morning; slight edema of the legs; heart's action was irregular; passed about ℥xxv of urine a day.

August 14: Discharged improved.

Temperature was normal most of the time; one or two slight rises to 101.4 F.; pulse 80 to 120.

Treatment.—Diuretics, nitroglycerin, warm baths, pilocarpin and saline enemata.

During the patient's stay in the hospital and after operation the urine varied in amount from ℥v to ℥l; sp. gr. 1,010 to 1,034, reaction acid, albumin + to ++; at times boiled solid; urea 105 to 310 gr.; microscopically very many casts, hyaline and granular. The last examination showed it pale in color, acid, sp. gr. 1,016, + for albumin, 0 sugar, 1.27 per cent. urea, 190 gr.; 33 ounces in twenty-four hours. The microscope revealed a few hyalogranular casts and bacteria.

Sept. 10, 1905, the patient was readmitted.

History Since Discharge.—Edema of face and extremities and the enlargement of the abdomen had increased. For about ten days the patient had fever and chilly sensations. For three days the previous week he had severe frontal headache. Slept well, appetite good; had been on a milk diet; bowels had three enemata a day; no vomiting; passed very little urine, which was high colored. The patient was weak, played about the house but not with the boys in the street; heart throbbed very strongly and at times he complained of palpitation. The three principal symptoms were, increasing edema, diminished urine, weakness and headache.

Physical Examination.—General condition good; child pale; slight dilatation of alæ nasi with respiration.

Face: Puffiness, edema of eyelids; edema of back.

Lungs: Anteriorly a few fine crepitant râles over right apex, extending down to third space, and in right axilla to fourth space. Posteriorly lung resonance extended to ninth rib in postaxillary line, on right side (two fingers below angle of scapula). Resonance descended on deep inspiration. On left side resonance extended to seventh space. Resonance descended on deep inspiration. At right apex were a few crepitant and subcrepitant râles. In both interscapular regions inspiration was slightly higher pitched and harsher than normal, and there were a few adventitious sounds. Breathing extended to two fingers below limit of resonance and there were a few subcrepitant râles at left base. Fremitus on right side extended to ninth space; on left side it was obscured by edema.

Heart: Apex beat not visible or palpable. Sounds best heard in fifth space, 8.5 cm. from median line.

R. B. in third space, 2 cm. from median line; in fourth space, 2.5 cm. from median line.

L. B. in third space, 7.25 cm. from median line; in fourth space, 9.25 cm. from median line.

U. B. third rib.

Second sound at apex accentuated and valvular. At base both sounds were accentuated, aortic more than pulmonic.

Pulse: Equal, irregular in force, some increased tension, no thickening.

Liver: Dull fourth space, flat fifth space, to free border; dull tympany one finger below free border; palpable 1½ fingers below free border; edge sharp and firm.

Spleen: Dulness eighth space, flatness ninth space to free border; spleen descended 1½ fingers below free border with deep inspiration; edge firm and rounded.

Abdomen: Lax; diastasis recti; no umbilical hernia; dull tympany in flanks which disappeared with change of position. There was a fluid wave obliterated by very slight median pressure. Circumference at level of imbilicus 63 cm.

Extremities: Moderate edema of legs.

September 11: Hgb. 74 per cent.; W. B. C., 19,800; R. B. C., 4,110,000.

September 13: Edema had increased; patient was not passing sufficient urine.

September 18: Edema was less; passing more urine; movable dulness in left flank; no fluid wave; circumference of abdomen 66 cm.

Edema increased again and then diminished. On November 15 there was no edema of extremities. Pallor was still marked; pulse tension not increased, and no signs of fluid in abdomen.

November 18: Patient had been absolutely free from symptoms referable to general well being for some time.

Temperature was normal most of the time. There were one or two rises. Pulse 70 to 120, respiration 24 to 28.

Treatment.—Hot packs, pilocarpin, fluids, salts.

Urine on admission was amber colored and clear, reaction acid, sp. gr. 1,024, albumin ++, 0 sugar, many hyaline and granular casts. No R. B. C.; few p. c. and epithelial cells; 3 per cent. urea and 129 gr. in twenty-four hours.

The urine improved, there was less albumin and more urea, but this varied; at times the urine was worse. At one time the urine boiled almost solid.

At discharge urine was straw colored, clear, acid, sp. gr. 1,022, albumin, a trace. Microscopically, very few hyalogranular casts; very few p. c. and epithelial cells.

March 31, 1911. The patient remained perfectly well for 4½ years after discharge from the hospital, then was exposed in October and chilled on the roof of school; took off his shoes. He then developed anasarca and for three months was in the hospital and recovered. Had been well since. Was 15 years of age, and weighed 91¼ pounds. He was in fine physical condition, had an excellent color, with no edema, no headaches, or any symptoms; pulse 84 tension, 110 to 120 mm. Hg.; urine sp. gr., 1,015; very few hyaline and granular casts of small caliber; passed 40 to 45 ounces of urine daily; albumin very marked; urea 0.018 to the c.c.; diet mixed; no meat, no eggs, no salt; took soup.

This patient was in the hospital three times suffering from the usual accidents of chronic nephritis. He had been partly relieved each time and discharged and returned with a recrudescence of symptoms. After the operation he improved very slowly, was removed from the hospital, returned and finally recovered completely. He remained well for four and one-half years, and then exposed himself on a roof barefooted in late winter and had a full recrudescence of symptoms. It took three and one-half months for these symptoms to clear up and he was then free from symptoms. He had probably a large kidney with a very large percentage of albumin and some isolated small caliber casts in the urine; urea normal. The patient had absolutely no symptoms. Anyone looking at the boy would think he was in rugged health.

The third case was that of a female child 8 years of age, admitted June 28, 1909, and died Aug. 26, 1909.

There was no history that could be traced as to heredity or exanthemata; she had a self-evident chronic nephritis as shown by operation.

On admission she had been five weeks ill with edema, vomiting and abdominal distention. There were remissions in the intensity of the edema; there were no headaches or convulsions or dyspnea before admission to the hospital. On admission to the service of my assistant (Dr. Henry Heiman) there was general anasarca involving both pleura; not the cardia, and with the hydrothorax there was also ascites. After admission she developed a petechial eruption.

After failure with other forms of treatment and Southey's tubes, convulsions set in a month after her stay in the hospital, and after repeated convulsions she was operated on August 20, fully seven weeks after admission. She never fully rallied from the operation. At the operation, performed by Dr. Elsberg, the right kidney was shown to be normal in size with an easily stripped capsule, the left to be enlarged and white, bulging through the incision in the capsule. An examination of a piece of the organ showed chronic parenchymatous nephritis.

The urine during the illness was loaded with casts, hyaline and granular, and leukocytes, which were also found after operation. The amount of urine passed in twenty-four hours was not measured.

This case is of great importance as it shows that we cannot rely on the operation to immediately restore the kidney to a power of functionating that is consistent with life, if this has been severely threatened. In all the cases thus far it will be seen that the kidney did not recover itself after operation until the wound had entirely closed, so that it cannot be that the extensive wound itself had anything to do with the relief of the patient, for anasarca did not disappear until the wound had completely closed.

Case 3.—C. B., female, aged 3 years.

Family History.—Negative.

Previous History.—No scarlet fever, no account of infectious diseases.

Present History.—Five weeks prior to admission, swelling of face, hands, etc.; vomiting a great deal; voiding small quantities. Under a physician's care the edema decreased, then increased. The abdomen became distended.

Physical Examination.—General anasarca; urinous odor to breath.

Lungs: Fluid in both chests; fluid in abdomen.

Von Pirquet test negative.

W. B. C., 26,000; polynuclears, 91 per cent.; leukocytes, 9 per cent.

Urine: Sp. gr. 1,010 to 1,040; albumin, heavy trace to ++; many casts and R. B. C.

Three days after admission a petechial eruption appeared over the abdomen; edema increased in spite of treatment. Southey tubes did not drain well. Necrosis of labia majora developed. Later necrosis spread to other parts of the vulva; erysipelatous eruption also appeared around vulva, which later disappeared.

July 30: Child had convulsions, followed by coma, which cleared up shortly.

Urine progressively decreased.

August 11: Paracentesis; 30 c.c. of clear fluid removed.

August 13: Child again in convulsions; temperature rose to 105 F.

August 18: Marked chemosis present; twitching of right forearm present for several days.

August 19: Edebohls' operation performed by Dr. Elsberg. Only left kidney showed "A large white kidney"; right kidney practically normal. After capsules were incised, parenchyma of both kidneys did not bulge and felt soft.

August 20: Since operation the child had not passed any urine, although edema was less marked; pulse good, and of very high tension; face twitched; petechial eruption over both ulnars.

August 21: Temperature subnormal—96 F.—in the morning.

August 23: Low several days; temperature was subnormal, barely rising to normal in the afternoon; at one time temperature was 94.4.

August 25: Child died. Urine did not increase; temperature rose above normal 100.6, and before death to 101 F.

Case 4.—J. M., male, aged 13.

Family History.—Negative; father 43, well; mother died at 33; cause unknown; four other children alive and well.

Past History.—Infancy normal; measles when 2 years old; diphtheria at 6 years—recognized when child had paralysis of palate following it; remained in Middlesex Hospital, London, for one week, and was discharged cured; no other acute infectious diseases; never before was in a condition like the present.

Present Illness.—Feb. 5, 1910, the child complained of headache, pain in the eyes, and nausea; no vomiting; some chilliness and fever; face became puffy, most marked around the eyes; child had also general discomfort and malaise; also cramps in the abdomen; edema of the feet was noticed February 9; child felt indisposed and had no appetite.

Physical Examination.—Feb. 10, 1910, examined by Dr. Hahn; general condition good; well nourished; marked edema around both eyes; edema about back of scalp.

Eyes: Edema around both eyes, pupils react; edema on back of scalp; movements normal; conjunctiva congested.

Mouth: Teeth and gums in good condition; throat clear; tonsils large; no paralysis of soft palate.

Head and neck: Glands not enlarged.

Chest: Lungs negative.

Skin: Edema of skin general.

Heart: Apex beat, fourth space, nipple line. Borders: Right at right sternal border; upper at second space; left in nipple line; action, regular, slow, forcible; second pulmonic reduplicated; no murmurs; pulse regular, large, slow, of moderate tension.

Liver: Fifth rib to free border; not felt.

Spleen: Not felt.

Abdomen: Somewhat distended, soft, tympanitic; edema of skin on abdominal wall and chest.

Extremities: Reflexes present; edema of both lower extremities; most marked on thighs.

Genitals: Normal.

Rectal: Not made.

Synopsis: Edema.

February 10: Fundi negative.

February 15: Edema increased in scrotum and lower extremities; urine gradually diminishing.

March 1: Patient complained of abdominal pain; edema of face increasing; large amount of edema in the back; signs of large amount of edema in the abdomen.

Lungs: Posteriorly, dulness and diminished breathing on right side beginning two fingers below the angle; on the left side two fingers above the angle.

March 21: General condition good; edema of face diminishing; there was marked edema of the back, abdominal wall, genitals, and lower extremities. There were signs of fluid in both chests beginning at the angle of scapula on right side and one space above angle on the left side; apex beat in fifth space, one finger outside the nipple; heart action regular and slow; second aortic sound accentuated; signs of fluid in the abdomen.

April 15: Patient this morning showed less edema of lower extremities; considerable edema of back and some puffiness of face; passed limited quantity of urine; patient's general condition not much improved after first week after admission; for past two months general anasarca stationary; secretion of urine sometimes increased; sometimes diminished under the most diverse management; no headache; confined to bed since admission.

Temperature, remained normal except on two occasions when it went to 101.4 F.

Operation.—In view of the absolute standstill condition and confinement of patient to bed and utter helplessness, an operation was advised and performed by Dr. Lilienthal, April 18, after a stay of eight weeks in the hospital.

April 18: Bilateral Edebohls performed in usual way, using fourth oblique incision in approaching kidney. Large "white" kidney found.

April 24: Abdominal distention did not show much change; face and legs greatly reduced; superficial dressings changed daily; always soaked with fluid.

April 30: Eyelids puffed.

May 4: Abdominal paracentesis done by Dr. Ryttenberg; 2,500 c.c. slightly turbid, yellowish white fluid removed.

May 13: Considerable edema of back below wounds; edema of face not so marked; temperature normal; wounds granulating.

May 14: Twenty-four-hour specimen of urine gave too much albumin to be measured by the Eschbach method.

May 18: Edema slowly increasing on thighs, scrotum, abdominal wall and back; much fluid in abdomen; slight edema of feet and legs; voided 600 to 700 c.c. a day; urine examination showed little improvement.

Urine Examination: Before operation, sp. gr. 1,010 to 1,020, pale, amber, clear; albumin present; very many hyaline and granular casts; R. B. C.; few W. B. C. Amounts of urine varied between 100 c.c. and 800 c.c. per diem. Amount immediately after operation, 615 c.c.; two days later, 1,500 c.c.; third day, 1,575 c.c.; fourth day, 1,100 c.c.; fifth day, 1,325 c.c.; sixth day, 1,500 c.c. From this time on the amounts diminished. On the twenty-first day the amount was 425 c.c. After that it varied between 600 and 825; on day of discharge it was 1,380 c.c.; albumin still +++; casts were moderate in number; few R. B. C.; many W. B. C.

May 1: Discharged to convalescent home.

Oct. 22, 1910, returned for examination; found in excellent condition, weighing 85 pounds; had been in good health all summer; no symptoms whatever; color good.

Urine: Trace of albumin, no casts. (Urine passed in office.)

Jan. 8, 1911: The patient had remained well; weighed 85½ pounds; urine + for albumin; sp. gr. 1,020; few hyaline and granular casts and leukocytes; arterial pressure 120 to 105.

March 14, 1911: Urine + for albumin; few small caliber casts, hyaline and granular; arterial pressure 120 to 110; weight 91 pounds; color excellent; in perfect health; no headaches.

This is really the most brilliant case of the series because improvement was coincident, within a few days, with the operation. The boy was well taken care of, protected from cold and on a very strict diet after the operation. He had never been in as good a condition of health and this freedom from symptoms continued to a year after operation. In this case also the urine still showed marked disease of the kidney, but the arterial tension was practically normal and there were no circulatory signs.

The fifth case in which operation was done is peculiar in that there was always a slight amount of general edema of the surface and the urine was diminished in amount, the patient confined to bed in a semi-soporous state, with no ambition, and nothing in the form of diuresis was of avail in increasing the amount of urine or in rousing the patient from his invalid state. After operation he improved, then relapsed, and finally permanently improved and remained well, being free from symptoms six months after the operation.

Case 5.—A. S., male, aged 5 years; in the hospital Oct. 11, 1909, to Jan. 23, 1910.

Family History.—Negative.

Previous History.—Measles at 2 years, no scarlet fever, or other account of infectious diseases.

Present Illness.—Began eight days prior to admission with edema of face and legs, diminished urination, headache.

Physical Examination.—Swelling and edema of face, eyelids, scalp and legs; eyes could not be opened on account of edema of eyelids.

Lungs: Showed fine moist râles in left base and both axillæ, flatness, distant breathing and voice from right of scapula to base.

Abdomen contained no fluid.

Urine: Hyaline and granular casts; trace of albumin; sp. gr. 1,016 to 1,030; acid, amber, clear.

Blood: Hgb. 94 per cent.

For a time edema decreased and urine output increased. Later the original conditions returned. About two weeks before discharge the patient received theobromin sodium salicylate (diuretin) for six days, increasing the urine output from 375 c.c. to 955 c.c.

On discharge the urine showed sp. gr. 1,006, heavy trace of albumin and a few granular casts; edema of body much decreased.

July 28, 1910, readmitted to hospital.

Physical Examination.—Marked edema around eyes; skin covered with small vesicles; edema of extremities; movable dulness in abdomen; fluid on both sides of chest.

August 1: Urine small in amount.

August 4: Prolapsus ani occurred and replaced.

September 5: General condition good; on general diet; edema much diminished; urine still small in amount; responded to hot packs.

September 18: Prolapsus of rectum reduced.

September 23: Fluid in abdomen increasing.

November 1: Urine showed exaggeration of nephritis under full diet and forced fluids.

November 10: In last six days, exacerbation of edema especially around face; urination scanty, 50 to 100 c.c. daily; showed slight evidences of uremia; no evidence of serous effusion anywhere.

Temperature in greater part varied between 98 and 100.2 F., occasionally rising to 104; pulse 100 to 120; respiration 24 to 28.

Blood: 98 mm. Hgb.

Urine, dark amber, clear, acid, sp. gr. 1,024 to 1,038; very heavy trace of albumin; many hyaline and granular casts; few R. B. C. and W. B. C.; this picture varied at times as the condition improved.

Hemoglobin, 65 per cent.

November 13: Operated on by Dr. Lilienthal. Four-inch lumbar incision made for extraperitoneal exposure. Fibrous capsule nicked and stuffed away; gauze packed around kidney. Kidneys showed "Large white kidney" of chronic parenchymatous nephritis. Operation lasted six minutes.

November 21: First dressing; gauze removed; kidneys less swollen.

December 3: For the previous few days the edema had increased; wounds healing.

Summary from day after operation to December 3: Immediately following operation the general condition improved, edema decreased, patient became noticeably brighter. This improvement remained for two weeks, after which edema increased and amount of urine decreased.

URINE EXAMINATION

Date	Amt. c.c.
November—	
13	25
14	160
15	115
16	190
17	165
18	220
19	125
20	125
21	150
22	715
23	520
24	515
25	435
26	505
27	525
28	370
29	395
30	225
December—	
1	350
2	200

At all times the urine contained a heavy trace of albumin; sp. gr. 1,014 to 1,024; many hyaline and granular casts.

Diet was forced fluids; total ℥l to ℥lxxx per day.

December 11: Under restricted diet and no medication, well marked diuresis was established. Urine amounted to 1,000 c.c. Hgb. 45 per cent.

January 16: General condition good; up and about; full diet; gaining in weight every week; no edema; voiding large quantities of urine.

January 27: Urine still contains casts; general condition good.

January 31: Urine is amber, clear; sp. gr. 1,016; faint trace of albumin and few W. B. C.

March 31, 1911: Four and one-half months after operation; has been out of hospital since January 31; is pale but has absolutely no edema. Weight 46 pounds.

Urine: Albumin very marked; quantity 7 parts *pro mille;* urea 1.8 per cent.; abundant hyaline, granular and epithelial casts.

In reviewing the five cases I wish to emphasize the fact that with the exception of Case 3 all were carefully selected for the procedure of Edebohls after I had failed with a reasonable trial of well-known internal methods. I think there are two facts which stand out quite sharply on the canvas, and these are, first, the absolute well-being of the patients in the successful cases for great lengths of time after operation, and this for greater periods than with medicinal agents in the face of continued signs in the urine of grave disease of the kidney persisting after the operation; and second, that, as in Case 2, the kidney if exposed after operation to exciting agents will give symptoms and still be able to recover itself as if no operation had been performed. In other words, the operation has not compromised the recuperative powers of the kidney.

Improvement does not set in immediately after the operation, as one would be led to believe, but only, it seems, after the surgical wounds have thoroughly healed and the kidney has become accustomed to the new local circulatory conditions. The well-being of the patient is more striking than after recovery from medicinal therapy. It is, as one would be led to believe from a study of Case 3, inadvisable to operate in the face of acute uremic symptoms.

30 East Sixty-Second Street.

PROGRESS IN PEDIATRICS

ACUTE INFECTIOUS DISEASES

Epidemic Cerebrospinal Meningitis

A Review of the Recent Literature

The discovery of the diplococcus intracellularis meningitidis by Weichselbaum, in 1887, led to a prolonged controversial discussion as to the organism's specifically for this type of meningitis. Bonomé, Jaeger and Heubner assumed either that more than one organism was concerned in the causation of this disease, or that the *Diplococcus intracellularis* did not show constant morphologic and staining characteristics. The final establishment of the claim of Weichselbaum that this organism is the sole specific agent of epidemic meningitis came recently with the development of bacteriology along the lines of specific reactions, more particularly the precipitin and complement fixation reactions. With the definite settlement of this important point in the etiology of the disease, other problems of great importance came to the fore.

Though meningitis, as shown by the name most commonly employed, has appeared in repeated and very extensive epidemics, the strange and apparently inexplicable phenomenon has often been observed that despite lack of isolation either at home or in public institutions, but few cases have been reported in which direct contagion could be traced. With the development of reliable methods for isolating the meningococcus, numerous studies have appeared on its presence in the nasopharynx of normal individuals coming in intimate contact with patients suffering from the disease.

Von Lingelsheim was one of the first to work along these lines, and his observations have been confirmed by Dopter, Bruns and Hahn, Bochalli, Selters, and others. Albrecht and Ghon have described epidemics of rhinopharyngitis due to the meningococcus, observed during an epidemic of meningitis. These facts and the postmortem findings of marked swelling of the pharyngeal tonsil and posterior part of the nasopharynx by Westentoefer in twenty-nine cases of meningitis, speak strongly for the nasopharyngeal route of infection. Dopter,[1] basing his views on his own observations and on those previously mentioned, denies the existence of such a condition as an epidemic of meningitis. It is more exact to speak of an epidemic of meningococcic rhinopharyngitis in the course of which a certain number of individuals develop meningitis as a complication. What determines the occurrence of this complication, whether it is the virulence of the particular strain of the organism, deficiency of the local or general immunity products in certain individuals, the physiologic or anatomic peculiarities of the vascular and lymphatic apparatus of the nasopharynx, or the seasonal influences, is at the present stage of our knowledge purely hypothetical. Work along this rather neglected field of research is urgently needed. Experimental meningitis has advanced to such a stage that it would seem as though some of these important problems were capable of solution. Moreover, granted that the nasopharynx is the primary portal of entry, we are still in doubt as to the route along which the meningococcus reaches the meninges. While many, Flexner among them, consider the lymphatic route the most probable, anatomic and pathologic studies on the lymphatic circulation of the nasopharynx seem to throw some doubt on this view. Bacteriologic studies of the blood in the very early stages of the disease have not been sufficiently numerous to be helpful in the solution of this problem.

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[1] Dopter: La Prophylaxie et la Traitement de la Méningite Cérébrospinale Epidémique, Jour. méd. Francais, iii, 106.

The symptomatology of epidemic cerebrospinal meningitis is so well established that little of novelty can be expected in the recent literature. Macgregor[2] in a paper on the immunity phenomena in this form of meningitis, divides the disease into three periods:

> *First Period:* Acute general infection with recovery by crisis, usually within the first week. Associated with this is a marked production of agglutinins proportionate to the severity, duration, and degree of reaction. The opsonic index becomes definitely raised within the first week.
>
> *Second Period:* There are present symptoms of local irritation, and the toxic phenomena such as emaciation, increased urea excretion and erythrophagocytosis are due to metabolic disturbances. Recovery takes place by lysis, usually within four weeks. The agglutinins in this period diminish, while the opsonins increase or continue high.
>
> *Third Period:* This is very chronic, with a variable temperature. The exudate is scanty, and the organisms persist in the cerebrospinal fluid. Agglutinins are absent, while the opsonic index remains as in the second period. Macgregor found no opsonins in the cerebrospinal fluid, even when they were abundant in the blood. Repeated removal of the fluid by lumbar puncture did not stimulate the formation of opsonins.

A notable study on the cerebrospinal fluid in the infective diseases of the meninges has recently been contributed by Connal.[3] Among other cases there were 152 of epidemic meningitis in which the character of the cerebrospinal fluid was carefully studied. The highest intracranial pressure was found in the early stages, in which reaccumulation of fluid takes place rapidly. Often it rises above normal within a few hours after a puncture. Increased pressure is a constant phenomenon and often persists for some time after subsidence of the disease. The normal transparency of the fluid is almost always lost, and the degree of turbidity indicates the extent of the exudate. A yellowish or greenish color in a turbid fluid is significant of a virulent infection. Organization or absorption of the exudate is shown by clearing up of the fluid, but as long as exudate is present, some degree of opalescence persists. The presence of a coagulum is one of the earliest signs of meningeal inflammation, and is the last to disappear. The alkalinity is reduced, due to the formation of lactic acid from the dextrose by the meningococcus. In the later stages of the disease, the meningococcus loses the power of converting dextrose into lactic acid, so that the alkalinity once more approaches the normal. The amount of albumin present is a reliable measure of the severity of the inflammatory process. The absence of a reducing sugar is pathognomonic of meningeal inflammation. The reappearance of sugar indicates, in most cases, beginning recovery. The polynuclears show marked increase, depending on the acuteness of the inflammation. Mononuclears predominate at the termination of the disease; these cells may persist for some time after convalescence. The presence of endothelial cells is also indicative of meningeal inflammation, their number being proportional to the severity of the inflammatory process. In acute cases, after the first few days, large numbers are found. The number of endothelial cells increases with extension or aggravation of the morbid process. At the termination of the disease they are seen in large numbers, sometimes cemented together. The presence of a large number of meningococci is an unfavorable sign; persistence of extracellular diplococci is seen in fatal cases. Death, however, may ensue even when all the organisms are within the cells.

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[2] Macgregor: Immunity Phenomena in Cerebrospinal Meningitis, Jour. Path. and Bact., xiv, 503.

[3] Connal: A Study of the Cerebrospinal Fluid in the Infective Disease of the Meninges with Special Reference to Cerebrospinal Fever, Quart. Jour. Med., iii, 152.

Netter and Debré have observed clear fluid either in the early or late stages of cerebrospinal meningitis, and in abortive cases. Not infrequently they found meningococci in clear fluid. The French observers consider the precipitin reaction of Vincent and Bellot and the fixation reaction of Bordet and Gengou of diagnostic value in the cases in which the meningococcus can not be found in the fluid. Kirchner found an agglutination reaction in the blood in 55.2 per cent. of his patients. It can readily be seen from his observations and those of Macgregor that the examination of the blood can not supplant that of the cerebrospinal fluid in the diagnosis of meningitis.

Salebert and Thurbert[4] describe the constant occurrence of polyuria associated with increased excretion of urinary constituents in patients with cerebrospinal meningitis. Similar observations are recorded by Apert and Griffon, Nattan Larrier, Loeper and Gouraud. The polyuria and the increase in nitrogen, chlorids and phosphates, and the occasional presence of glycosuria are assumed to be due to irritation of the centers in the medulla, and are considered pathognomonic by these French observers.

The therapy of epidemic meningitis was, until recently, one of the most unsatisfactory in the whole field of medicine. Despite all kinds of symptomatic remedies, despite repeated lumbar punctures, so highly lauded at one time, despite intradural lysol injections, subcutaneous injections of diphtheria antitoxin, and the use of vaccines, the enormously high rate of mortality remained unchanged from year to year. With the opportunities for experimental work presented by the recent epidemics in the United States, Germany, and France, the therapy of this disease entered a new phase. Practically simultaneously, Kolle and Wassermann, Jochmann and Flexner prepared antisera which, from their effect on experimental meningitis, justified the hope that a valuable therapeutic agent had at last been discovered. Applied subcutaneously, as was first done in Germany, it was soon found to be of no value in this manner of application. To Flexner belongs the lasting credit of insisting from the first on its intralumbal application. He argued that if the serum is to be effective, it must come in contact with the meningococcus in a concentrated form, and this could be accomplished only by injecting the serum directly in the spinal canal.

The details of the mode of preparation of the serum can not here be given; suffice it to say that Flexner prepares his serum by injecting a horse once a week alternately with dead cultures and autolysate of many strains of the meningococcus. In the course of eight months a sufficiently potent serum is derived.

By a wise mode of distribution, permitting the use of the serum by trained observers only, Flexner soon obtained sufficient data indicating the value of this mode of treatment. In his most recent paper[5] he reports on 712 collective cases, showing a mortality of 31.4 per cent. The appended table from his paper shows the mortality at various age periods:

Age, Years	Cases	Mortality, Per cent.
1-2	104	42.3
2-5	112	26.7
5-10	113	15.9
10-15	101	27.7
15-20	107	32.7
Over 20	175	39.4

According to Dopter[6] 158 patients treated with the Kolle-Wassermann serum by Krohne, Levy, Hahn, Tobben and Grocco, yielded a collective mortality of

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[4] Salebert and Thurbert: Syndrome Urinaire Paradox Rev. de méd., xxx, 205.

[5] Flexner: Antimeningitis Serum and the Results of Its Employment, Internat. Clin., Series 19, iv, 1.

[6] Dopter: La Sérothérapie Antiméningococcique, Ann. de l'Inst. Pasteur xxiv, 96.

18.35 per cent. Krohne[7] reports on serum treated patients who came under his observation in the gubernatorial district of Düsseldorf. He injected intraspinally the Kolle-Wassermann serum in twenty-two cases with six deaths, a mortality of 27.3 per cent.

E. Levy[8] employed the Kolle-Wassermann serum given intraspinally in twenty-three cases in the barracks at Essen; there were five deaths, a mortality of 21.74 per cent.

Holm[9] used the same serum and technic at Essen in forty-one cases with five deaths, or a mortality of 12.1 per cent.

Többen[10] treated twenty-nine patients similarly at Bochum with a mortality of 34.5 per cent. In twelve of these cases, in which treatment was begun on the first or second day of the disease, the mortality was only 16.6 per cent.

E. Grocco[11] used the same method and serum at Milan in ten cases, with two deaths, or a mortality of 20 per cent.

Schoene, using the Jochmann serum, obtained a mortality of 27 per cent. Dopter reports on 402 patients treated with a serum prepared by him at the Pasteur Institute, in which the mortality was 16.44 per cent. Excluding seventeen cases injected but a short time before death, two cases in which death was due to other causes, and nineteen other cases excluded for other valid reasons, he derives 383 cases with only forty-seven deaths, a mortality of 12.27 per cent.

A comparative table of mortality at various ages as obtained by Flexner (an earlier report), Netter[12] (Flexner's serum), and Dopter, gives the following instructive data:

Age Years	Flexner, Per cent.	Netter, Per cent.	Dopter, Per cent.
Less than 1	50.0	50.0	48.6
1-2	42.1	0 (6 cases)	20.1
2-5	23.5	16.6	9.3
5-10	11.4	12.5	8.5
10-20	23.8	0 (8 cases)	10.2
Over 20	26.4	0 (8 cases)	14.1

Even more instructive is the table giving the mortality rate with reference to the time of injection:

Time of Injection	Flexner, Per cent.	Netter, Per cent.	Dopter, Per cent.
Before third day	14.9	7.14	8.20
Fourth to seventh day	22.0	11.1	14.4
After first week	36.4	23.5	24.1

The importance of early injections is here strikingly shown.

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[7] Krone: Ueber die bisherigen Erfolge der Behandlung der epidemische Genickstarre mit Genickstarre-Heilserum in Regierungsbezirk Düsseldorf, Ztschr. f. Med., Beamte, Berlin, 1908, xxi.

[8] Levy, E.: Erfahrungen mit Kolle-Wassermannschen Meningokokken-Heilserum bei 23 Genickstarrekranken, Klin. Jahrb., Jena, 1907-08, xviii.

[9] Holm: Die Ergebnisse der bakteriologischen, cystologischen und chemischen Untersuchung der Lumbalexudate von 37 Genickstarrekranken unter dem einfluss des Kolle-Wassermannschen Meningokokkenserums, Klin. Jahr., Jena., 1908, xx.

[10] Többen: Zur Therapie der Meningitis cerebrospinalis epidemica, München. med. Wchnschr., 1907, liv, No. 49.

[11] Grocco, E.: Sopra dieci casi di meningite cerebro-spinale epidemica, Gazz. d. osp., Milano, 1909, xxx.

[12] Netter: Rareté de Séqueles ches le Sujets guéris de Méningite Cérébrospinales, à la suite des Injections intrarachidiennes de Sérum antiméningococcique.

Unfortunately, there is at present no unanimity as to the dosage and the details of the serum therapy. Some authorities advise the use of one dose which is to be repeated as often as improvement has become arrested or a relapse has taken place. Dunn[13] has worked out a plan of treatment which those who have not had a large personal experience with the serum would do well to follow. He advises the use of a full dose as soon as cloudy fluid is obtained, without waiting for a bacteriologic examination. The dose should be 30 c.c. if that much can readily be introduced, and as much serum as fluid withdrawn if more than 30 c.c. has been removed. In very severe or fulminating cases, the serum should be reinjected as soon as the patient begins to get worse, or at twelve-hour intervals. In the average case the injection should be repeated daily until four full doses have been given. If the diplococci persist in the fluid after four days' treatment, the injections should be continued until the organisms have disappeared. If subjective symptoms, such as mental impairment or fever, persist after the diplococci have disappeared from the fluid, or after four full doses have been given without progressive improvement, four days should elapse before another course of four daily treatments is begun. When a relapse occurs or meningococci reappear in the fluid, the same treatment should be adopted as for the original attack. In the chronic stage, reappearance of meningococci should lead to the institution of treatment as for an acute attack. In chronic cases with excessive fluid not containing meningococci, daily punctures should be done, but serum should not be injected.

Dunn's[14] figures obtained by following the above outlined method of treatment are very instructive. He compares the mortality at the Boston Children's Hospital previous to 1908 with the results obtained in that year, when serum was first used. Previous to 1908, symptomatic treatment, frequent lumbar punctures, frequent administration of diphtheria antitoxin and vaccines were successively used. The mortality during these years varied from 58 to 80 per cent.; in 1908 on the adoption of serotherapy it fell to 19 per cent.

Sladen[15] in a very thorough and detailed report of the cases (which were all sporadic) at the Johns Hopkins Hospital, shows that there were thirty-three cases up to 1908, with a mortality of 66.6 per cent.; in 1908 there were twenty-three cases with a mortality of 17.4 per cent.

According to Dunn, the effect of the serum is shown most often by a fall in temperature, which is often critical in character. There is rapid improvement in the general condition, consciousness returns, mental dulness disappears. Delirium, headache, hyperesthesia, tenderness of the neck and vomiting are often relieved in twenty-four hours. The rigidity of the neck and Kernig symptom often persist when all other symptoms have disappeared.

Simultaneously with the improvement in the symptoms, the following changes are observed in the cerebrospinal fluid. Within twenty-four hours the diplococci become much less abundant, the majority of the organisms being enclosed in the cells. They show signs of degeneration such as swelling of the protoplasm, feeble staining power, and impaired growth on culture media. After three days there are frequently no meningococci to be found. Not only is the mortality reduced, but the disease is considerably shortened. Moreover, there is a remarkable reduction in the frequency of complications and sequelæ when treatment is begun at an early stage. Flexner reports complications in only 2.56 per cent. of his cases, Netter in 7.5 per cent., and Dopter in 6.2 per cent.

Death is due either to the great severity of the initial infection or to secondary pathologic processes. As concentration is essential to effective action of the serum, the futility of intraspinal injection, when the process is chiefly localized in the brain, can readily be seen. In these cases, it has been proposed to inject serum directly into the ventricles, either through the fontanelle, or, in older children, through a trephine hole. Several successful cases are reported in the literature. When local complications occur; such as arthritis, serum should be injected locally (as was done successfully by Ladd).

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[13] Dunn: The Serum Treatment of Epidemic Cerebrospinal Meningitis, Jour. South Carolina Med. Assn., x, 315.

[14] Dunn: Cerebrospinal meningitis, Am. Jour. Dis. Child., 1911, i, 95.

[15] Sladen: Epidemic Meningitis and Serum Therapy at Johns Hopkins Hosp., Johns Hopkins Hosp. Rep., xv, 307.

The mode of action of the serum is assumed by Flexner[5] to be chiefly bactericidal. It injures the meningococci in such a way as to limit their multiplication and cause rapid disintegration and death. Phagocytosis is greatly increased by the serum. The phagocytes not only destroy the organisms, but also exert a neutralizing effect on the endotoxin, thus preventing injury to the body by too rapid liberation of endotoxin.

The residuum of mortality even with the most skillful use of the serum is still so considerable that unremitting search for efficient prophylactic measures is far from dispensable. The frequency and persistence of meningococcus in the nasopharynx of healthy individuals shows that this will prove to be a task of considerable difficulty. Schubert, according to Selter,[16] found 391 meningococci carriers among 2,025 school children. Various observers have found meningococci in the throat for periods ranging from one week to several months, and the father of one of Selter's patients showed the meningococci in the nasopharynx for at least seven months. Though v. Lingelsheim found that the meningococci usually disappear within fifteen days, there are cases in which they persist indefinitely. These facts clearly indicate that isolation of these "carriers," except under exceptional circumstances, is impracticable. Unfortunately, up to the present time, most of the measures advised and used with the aim of rapidly destroying the meningococcus in the throat, such as insufflation of dried antimeningococcus serum, the use of pyocyanase, and the various local antiseptics, are devoid of effect.

Recently, Vincent and Bellot have advised the adoption of the following plan of treatment. Daily painting of the tonsils and pharynx with iodin in glycerin, 1 to 30, frequent gargling with hydrogen peroxid to 1 to 10, and inhalation four or five times a day of the following mixture:

Iodin	20.0
Guaiacol	2.0
Thymic acid	0.25
Alcohol (60 per cent.)	20.0

With this mode of treatment, Schneider[17] found that there was no growth after four days. Other French observers also recommend this mode of treatment.

Numerous as are the gaps in our present knowledge of cerebrospinal meningitis, the important contributions of the last decade, in which America has played a decidedly gratifying part, justify the hope of an early conquest of this dread disease.

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TUBERCULOSIS AND SYPHILIS

Boston's Hospital School for Tuberculous Children

(*Edwin A. Locke and Timothy J. Murphy: Boston Med. and Surg. Jour., Aug. 17, 1911*)

In July, 1908, the Boston Association for the Relief and Control of Tuberculosis opened a day camp for tuberculous children. The children were kept in the open air for the entire day, and were always under a definite program, including the care of gardens, housework, play, rest, talks on health, and Nature studies. Later, the day camp was changed to an outdoor school and installed in the refectory building in Franklin park. The roofgarden was equipped with canvas curtains, to be used in case of storm or high winds, desks, chairs, etc., and converted into a schoolroom. Here the children remained during the day throughout the entire winter in spite of the hardest storms and coldest weather. All teachers were furnished by the School Department, and held to the same requirements regarding general work as in the ordinary public schools. The children, however, were regarded strictly as sick children, and their entire life in the school regulated in accordance with orders of the visiting physician.

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[16] Selter: Verhandl. d. Gesellsch. deutsch. Naturforsch. u. Aerzt., 1909, Part 2, No. 2, 577.

[17] Schneider: Prophylaxie de la Méningité Cérébrospinale Epidemique et désinfection du Rhinopharynx, Bull. et mém. Soc. méd. d. hop. de Paris, xxix, 192.

At entrance, each child was assigned a number and provided with a reclining chair, blankets, thick overcoat, paraffined canvas bag with a detachable blanket lining in which to sit or recline, woolen cap, mittens, overshoes, individual drinking-cup and toothbrush; all of which were numbered. By arrangement with the school nurses, all debilitated, anemic or undeveloped children were singled out, examined by the school physicians, and all positive or suspected cases referred by them to the Out-Patient Department for diagnosis. Many children from tuberculous families were also sent for examination by the nurses of the department. Other agencies have cooperated in making this dispensary the center for this special work. In consequence, the children admitted to the Hospital School were referred from this source, although a few were accepted on the recommendation of their family physician. The school was kept open on Saturdays and holidays, experience having demonstrated the bad results of repeated regular absence from the routine of treatment.

By special arrangement, all specimens of sputum and throat culture were examined in the city laboratory. A specimen of sputum from every child, so far as it could be obtained, was sent to the laboratory, and if negative, the examination repeated at weekly intervals. In all, sputum was obtained from but thirty-eight children; tubercle bacilli were found in nine. A culture was made as a routine of all cases of sore throat, and the child isolated at home under the care of the visiting nurses until the report of the examination was known. Likewise, all cases in any way suspicious of the acute exanthemata were sent home and kept under observation until the condition could be safely regarded as non-contagious. In spite of the fact that during the course of the last year several cases of contagious diseases appeared among the children, these rules were so carefully carried out that no case of contagion occurred. The nurse was furnished with written instructions covering all possible emergencies. One of the visiting physicians was always on telephone call, and every medical question of importance referred to him. Three physicians were regularly in attendance, as a rule at least four visits each week being made. Once each month every child was given a complete physical examination. The daily observations regarding the condition of the children were left to the nurse. Those children needing examination of the nose, throat or ears were referred to the Out-Patient Department. Other special conditions were treated in special clinics. Every effort was made to investigate the homes and to improve the conditions so far as possible when unfavorable.

The entire staff of the institution comprised three physicians, a nurse, social worker, dietitian, five teachers, a cook, two maids and a janitor. The Hospital School was in the strictest sense a hospital, organized and administered as such. It was not maintained for the "debilitated" or "anemic" child, but for the tuberculous only. At entrance the physical condition of the child was determined by one of the visiting physicians, and depending on this, he was placed in one of three groups. The daily program for each of these groups was arranged with reference to the amount and nature of the study, exercise and work. Those in Group I were required to follow the regular routine of the school, which included a systematic assignment of work, exercise and study. In Group III no work and a minimum of study and exercise was permitted. Group II was intermediate. Individual exceptions were, of course, frequently made. Absolute rest in the case of those with active tuberculosis was less rigidly enforced than would be considered wise in the treatment of adults.

Work of various kinds under supervision was arranged and graded so far as possible to suit the ages and fitness of children to perform it. In small groups the available children were assigned for each week to a schedule of duties. These consisted in setting and clearing the tables, washing dishes, sterilizing the eating utensils, dusting, assisting the nurse, watering the flowers, and other such occupations. On their arrival, at 8:15 a. m., the children first washed their hands and prepared for breakfast, which was served at 8:30. At 9, all the children were required to go to the wash room to brush their teeth. Those not assigned to work then went to the open-air room on the roof, where they were given breathing exercises and school work according to their condition. A few of the sicker patients remained in their steamer chairs for the greater part of the time. During the cold weather the school routine was frequently interrupted by short periods of light exercise. From 11:30 to 12, games were allowed. At noon school work ceased and the children prepared the roof for the rest hour. They then filed to the wash room to prepare for dinner at 12:30. Following dinner, the teeth were brushed and all basins and other utensils used in the wash room packed in the sterilizers. By 1:30 they were again in their places on the roof, where they rested in steamer chairs until 3. In the winter the children were kept warm during this period of rest by sleeping bags and blankets. At the close of the rest period exercises, singing, talks by nurses or teachers, and similar exercises occupied the time until 3:30, when the temperatures were taken and the chairs put away. By 4, they had again finished with the same preparations for the table, and sat down to supper. Beginning at 4:30, they were dismissed in small groups, a teacher accompanying them as far as the Dudley Street Transfer Station. On Saturdays and holidays, and during the summer, the teachers not being present, the work of the school was considerably changed. Volunteer workers took them for walks, supervised them in games, gave them talks on Nature or hygiene topics.

The children were not allowed to use ordinary handkerchiefs while at school, but were furnished with paper napkins instead, which, after being used, were placed in paper bags and at the end of each day burned in the furnace.

The closest attention was given to the question of nutrition. At intervals the children brought lists of the food eaten at home for a period of several days, and in the diet prescribed every effort was made to supplement this diet in such a way as to provide a total suited to the particular needs of the individual child. So far as possible, the food served was of the kind which can be provided by the families of the class from which the patients were drawn. A minimum cost was also a determining factor in its selection. This department was entirely in the hands of an expert dietitian, who devoted her entire time to the work. Throughout the year experiments were carried out on selected groups of children to determine the diet best adapted to their needs.

The following menu, calculated with reference to the calories furnished, is an illustration of the average diet.

Breakfast: Cocoa, graham gems and butter, stewed prunes.

Luncheon: Baked beans and brown bread, milk, apple or orange.

Supper: Milk, bread with jelly.

During the first ten months of the year 1910, with an average attendance of 64.25, the average cost of raw food materials per child per day was thirteen and one-fifth cents.

One of the most important features of the work in the Hospital School was the system of bathing carried out. Each child was supplied with an individual basin, soap, toothbrush, mug and comb, all of which, as in the case of the blankets and other articles mentioned above, were marked with the registration number. For the proper care of these the patients were held strictly responsible. Once each week, with few exceptions, every member of the group of children was required to take a shower bath, the teachers usually assisting the nurse in the work of supervision. Paper napkins were used in the place of hand towels, and tooth picks for nail cleaners. After being used both were burned in the furnaces.

The first cost of equipment was as follows:

Blankets, clothing, etc.	$1,208.21
Household, kitchen and dining-room supplies, hardware and equipment	1,065.51
Furniture and furnishings	357.75
Repairs	158.97
Electric fixtures	50.33
Plumbing	43.96
Medical equipment	14.66
Total capital expenses for school	$2,899.39

For the year 1910-11 the total general operating expenses were $8,231.60, or a cost per patient, per day, of 56 cents. This is exclusive of the School proportion of the general hospital administrative expenses, estimated as $1,277.34, which if added brings the per capita cost per day to 65 cents.

The general results of treatment have, on the whole, been extraordinarily satisfactory. From Oct. 12, 1909, when the Hospital School was taken over by the Boston Consumptives' Hospital, until its close, Jan. 31, 1911, a total of 191 children, ninety-four boys and ninety-seven girls, were treated. One hundred and seventy-four of these were treated during the year ending January, 1911. The patients classed as Stage 1 comprise 66 per cent., those as Stage 2, 24 per cent., and those as Stage 3, 6 per cent. of the total.

Tabulation of the 184 cases, comprising those actually tuberculous, according to the results of treatment shows the following:

	Arrested	Improved	Unimproved	Unknown	Non-tuberculous	Totals
Stage 1	51	53	8	11	4	127
Stage 2	13	23	7	1	1	45
Stage 3	0	6	5	1	0	12
Totals	64	82	20	13	5	184

The "unimproved" were chiefly of two groups: First, those who were too sick to be at the school, having been admitted because no place in a hospital could be provided for them; and second, those who attended for only a short period or very irregularly. The closing of the school further made it necessary to discharge all patients, irrespective of their conditions. About one hundred were registered at the school just before its closing. Fred C. Zapffe.

METABOLISM AND NUTRITION

Indicanuria in the New-Born

(*A. v. Reuss: Ztschr. f. Kinderh., 1911, iii, Part 1, p. 12*)

Von Reuss, working in Schauta's clinic, examined, for indican, 400 specimens of urine from breast-fed children without discoverable abnormality, especially with no infections or intestinal disturbances, in the first nine days of life, with the result that he found indican in from 14 to 42 per cent. of cases, none being found on the first or ninth days, and the largest proportion, 42.1 per cent., on the fourth day. He sums up his conclusions as follows:

Indican is quite frequently found in the urine of breast-fed children in the first week of life, sometimes in notable amount, without the presence of any pathologic conditions that are clinically observable.

It is found in children in good condition, as well as in those failing to increase in weight, in those having frequent evacuations of the bowels as well as in those having a tendency to constipation, and in those taking a scanty amount of food as well as those taking food abundantly.

The indicanuria, as a rule, is lacking on the first day, rare on the second, and is most frequently and abundantaly found on the third and fourth days; but it is not a rare occurrence during the following days.

Two possibilities must be considered with reference to the cause of this indicanuria. Although the meconium and the stool from breast milk show no signs of putrefaction in the intestine, still the occurrence of putrefactive bacteria makes it possible that there is a formation of indol from the intestinal secretion as the cause of the indicanuria. On the other hand, if the assumption of a parenteral origin of the urinary indican is admitted, the indicanuria of new-born children may be taken as an evidence of tissue destruction and may be brought into relation with the other well-known symptoms of such a process. Possibly also the increase of uric acid in the organism of new-born children plays a rôle in the production of indicanuria. These questions need further elucidation.

ACUTE INFECTIOUS DISEASES

Streptococci in Scarlet Fever

(*Felix Schleissner: Ztschr. f. Kinderh., 1911, iii, Part 1, p. 28*)

Schleissner, working in the pediatric clinic of the Franz Josef Children's Hospital and in the serologic department of the Hygienic Institute of the German University at Prague, reviews the relations of streptococci to scarlet fever, and shows that it has been proved that streptococci are present very abundantly in the throats of scarlet fever patients, and also in a large number of cases in the blood. He discusses the question as to whether they are related in an etiologic way to the disease itself or whether they are to be regarded as an evidence of mixed infection. The methods by which it has been attempted to prove an etiologic relationship are discussed. Three principal methods have been relied on—the power of the blood serum to agglutinate streptococci, the complement-binding principle, and the bactericidal power of the leukocytes. These methods have been used to show that there is a difference between the streptococci found in the blood in scarlet fever and the ordinary streptococci which produce septic manifestations.

In order to arrive at an opinion as to whether the presence of streptococci in the blood indicates a mixed infection, the author examined the histories of cases in which a bacteriologic examination of the blood had been made, with a view to determining whether there was any relation between the course of the fever and the presence of streptococci in the blood. He reasoned that if the presence of streptococci indicated a mixed infection, those cases in which the streptococci were not present would run a milder course than those in whicn the streptococci were found. The result of this investigation, however, was negative. Schleissner sums up the results of his investigations as follows:

In the investigation of 108 cases of clinical scarlet fever streptococci were found in the blood during life sixty times, or 55 per cent. Of these streptococcic cases, 31 per cent. of the patients had complications, and of those patients free from streptococci, 35 per cent., no connection of the complications with the presence of the streptococci in the blood could be shown.

While formerly by means of bacteriologic methods (agglutination, complement-binding and bactericidal principles) numerous differences between the streptococci of scarlet fever and of sepsis have been noted, it has now also been possible to show that in the blood-serum of patients affected with sepsis immune bodies active against the scarlet fever streptococci were not present, while in the serum of scarlet fever patients they were constantly found. From this the assumption of an essential difference between scarlet fever streptococci and septic streptococci becomes still more probable.

In the scales from various stages of desquamation streptococci could not be demonstrated with certainty microscopically nor by means of cultures. By a comparative examination of the temperature charts of scarlet fever patients it appears that the connection between the course of the fever and the presence of streptococci does not exist.

To set aside the etiologic importance of streptococci and to assign to them a really secondary rôle appears from these experiments not warranted at present.

The facts so far presented are insufficient to furnish exact proof of the etiologic connection of streptococci with scarlet fever.

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The annual meeting of the American Association for the Study and Prevention of Infant Mortality is to be held at Chicago, Nov. 16-18, 1911. The work of the Association will be transacted partly in small sections devoted to special work and partly in larger meetings of a popular nature.

There will be reports on infant welfare work in this country and abroad by Professor C. R. Henderson of Chicago, Dr. Hastings H. Hart, Director Department of Child Helping, Russell Sage Foundation, Assistant Surgeon General J. W. Kerr, U. S. Public Health and Marine-Hospital Service, and others.

The sections with their chairmen are as follows:

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A DISCUSSION OF MIKULICZ' DISEASE, WITH REPORT OF A CASE OF LYMPHATIC LEUKEMIA IN A CHILD WITH MARKED ENLARGEMENT OF THE SALIVARY GLANDS

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In the year 1892 Mikulicz[1] described a new disease, characterized by chronic, bilateral, painless enlargement of the lacrimal and salivary glands. In the cases which formed the basis of his report the blood was normal and there was no involvement of the lymph-nodes or spleen. The histologic picture resembled that of a lymphoma. There was no tendency to recurrence after complete extirpation. Mikulicz considered the disease to be due to some inflammatory agent of unknown nature.

Since then, however, cases have been reported in which pseudoleukemia or leukemia was accompanied by a similar enlargement of the lacrimal and salivary glands, and v. Brunn[2] in 1905 was able to collect a series showing all gradations from the syndrome described by Mikulicz to pseudoleukemia and leukemia. The association with the last-named disease, however, is so rare that the following case seems worthy of record.

Lymphatic leukemia of the "aleukemic" type, in a child 2 years old: large tumors of both parotid and both submaxillary glands, lacrimal glands not involved; autopsy.

History.—G. H., born Oct. 13, 1903, entered the Children's Hospital, Boston, Aug. 30, 1905. The baby was well till April, 1905, when she had fever, ranging from 103 to 105 F., for a period of three or four weeks. About three weeks after the temperature became normal, the parotid glands began to swell. Tincture of iodin applied over the glands caused them to decrease in size until they were scarcely noticeable by August 1, but the swelling soon returned. Bunches in the neck appeared three months prior to admission. There had been diarrhea, off and on, for two months previous to admission. I saw the child in the outpatient department of the Children's Hospital, and sent her into the hospital in the service of Dr. J. L. Morse, to whom I owe thanks for the privilege of reporting the case.[3]

Physical Examination.—The child was well developed and nourished and only slightly pale, and weighed 26¼ pounds. The appearance of the face was striking, resembling a very marked case of mumps. Palpation revealed a hard swelling of both parotid glands, about the size of hens' eggs. The skin over the tumors was not reddened nor adherent, there was no pain and no tenderness on pressure. A short distance in front of the parotid on each side was a hard mass the size of a marble. (Accessory parotid glands.) Both submaxillary glands showed similar swellings the size of walnuts. The lacrimal and sublingual glands were not enlarged. There was no exophthalmos. The tonsils were considerably increased in size, but without exudate or ulceration. The lymph-nodes in the neck, axillæ and groins were considerably enlarged. The examination of the chest was negative except for slight dulness over the upper part of the sternum. The liver reached from the fifth rib to 5 cm. below the costal margin in the nipple line; the surface was smooth and the edge hard and sharp. The spleen was much enlarged, reaching from the sixth rib to 5 cm. below the costal margin, the long diameter being 12.5 cm. On the outer side of the leg were several small ecchymoses. There was no edema and the signs of rickets were absent.

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[1] Mikulicz, J.: Beitr. z. Chir. Festschr. (Billroth), 1892, 610.

[2] Von Brunn, M.: Beitr. z. klin. Chir., 1905, xlv, 225.

[3] This case has been reported in brief by Dr. J. L. Morse: "The Anemias of Infancy," Jour. Am. Med. Assn., 1909, lii, 455, Case 17. (For the earlier history I am indebted to Dr. J. W. Clarke of Attleboro.)

Urine: Acid; no albumin, sugar or casts, but many leukocytes.

Blood: August 30, red cells, 6,860,000; hemoglobin, 95 per cent., leukocytes, 14,700; small mononuclears, 50 per cent.; large mononuclears, 23 per cent.; polynuclear neutrophils, 25 per cent.; eosinophils, 1 per cent.; basophils, 1 per cent.; no poikilocytosis and no nucleated red cells. September 1, red cells, 6,188,000. September 12, leukocytes, 11,500; small mononuclears, 51 per cent.; large mononuclears, 26 per cent.; polynuclear neutrophils, 21 per cent.; basophils 2 per cent. September 14, leukocytes, 6,700; small mononuclears, 23 per cent.; large mononuclears, 41 per cent.; polynuclear neutrophils, 36 per cent. The child was in very fair condition, with a slight fever, till September 14, when the temperature suddenly rose to 106 F., and she died the next day.

Autopsy.—(Dr. C. W. Duval.) There were dull purple spots on the thighs, upper arms and forehead, averaging 5 cm. in diameter. The parotid and submaxillary glands were much enlarged and firm. The cervical, mediastinal and mesentery lymph-nodes were considerably enlarged, ranging in size from that of peas to hazel-nuts. The thymus gland was greatly enlarged, measuring 8 cm. in its long diameter. The heart and lungs were not remarkable. The spleen was very large, measuring 18 by 7.5 cm.; it was firm and purplish red, and on section showed small grayish-white areas the size of a pinhead or less. The liver was enlarged and smooth and rather soft; on section mottled grayish-yellow and light red. The gastro-intestinal tract was normal. The kidneys were large, the capsule greatly thickened and showing considerable hemorrhage on its inner surface. On section the cortex was yellowish-white with many small hemorrhagic areas. Scharlach R showed a moderate amount of fat in the convoluted tubules.

Microscopic Examination.—(W. Tileston.) All sections were stained with eosin and methylene blue.

Salivary Glands: The parotid and the submaxillary glands presented identical appearances. The acini were widely separated by dense masses of cells of the lymphocytic series, which will be alluded to hereafter as lymphoid cells. The secretory cells appeared normal, except that they were crowded together so that no lumen was visible, suggesting compression. In places, especially near the capsule, there was a diffuse infiltration with lymphoid cells, and no gland-cells were seen. The capsule was thickly infiltrated with lymphoid cells. The connective tissue septa appeared increased in thickness, but were poor in cells.

Lymph Nodes: Sections of three lymph-nodes all showed similar changes. There was a general overgrowth of lymphoid cells, obscuring the normal structure. Only a very few normal follicles could be found. There was a considerable number of large cells with pale pink protoplasm and large vesicular nuclei (endothelial cells). One section showed infiltration of the adjacent fat tissue with lymphoid cells.

Bone Marrow: The bone marrow of the sternum showed lymphoid infiltration. Further details are not available because the section was lost before it was carefully studied.

Thymus Gland: The thymus showed a general overgrowth of lymphoid cells. Hassal's corpuscles were apparently diminished in number.

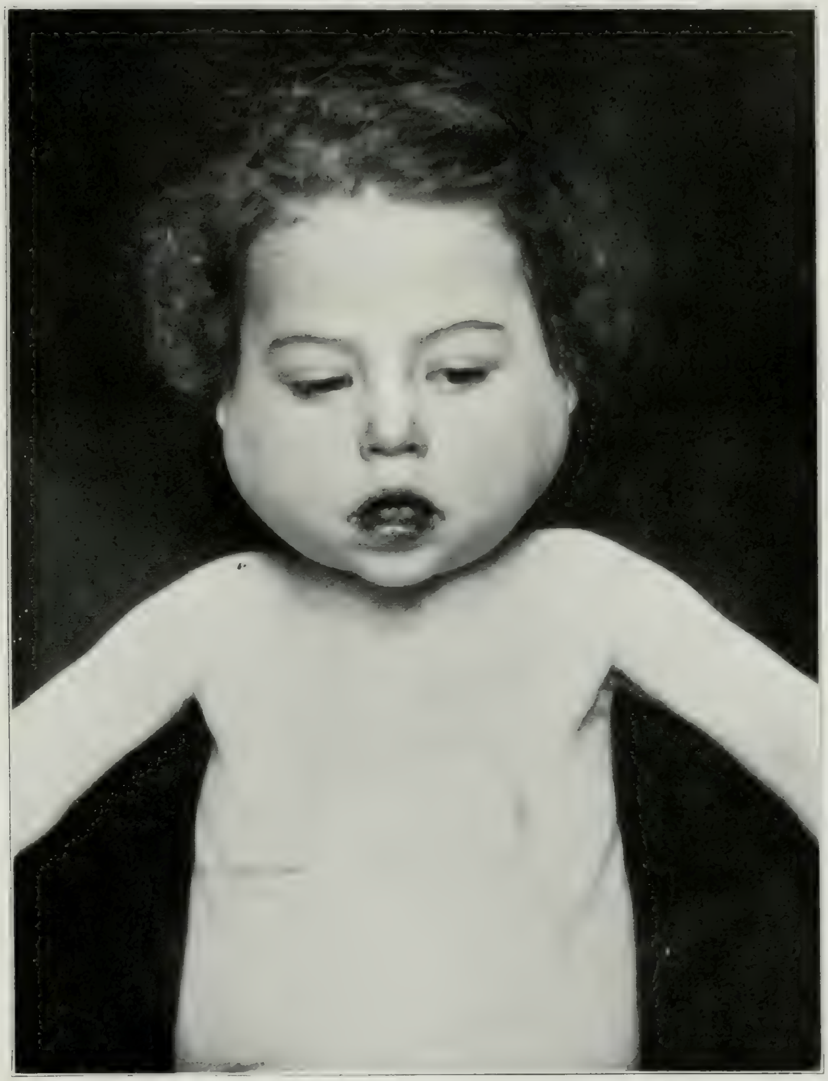

Fig. 1.—Photograph of author's case, showing the enlargement of the parotid and submaxillary glands.

Liver: The liver presented a remarkable degree of infiltration with lymphoid cells, involving the whole organ, but most marked about the portal vessels. This infiltration was mostly diffuse, but in places, especially in the portal spaces, there were large foci of lymphoid cells. Here and there a clump of these cells might be seen to lift up the endothelium of a central vein. In some places a blood-vessel was clearly separated by an endothelial wall from a mass of lymphoid cells: the latter, therefore, as Dr. Mallory pointed out to me, were situated in a lymph-sinus. The parenchymal cells were normal, except for some compression and atrophy.

Spleen: There was a striking infiltration with lymphoid cells along the larger vessels and next to the trabeculæ; the blood-sinuses were engorged with red cells. The follicles were enlarged, and some of them showed proliferation of endothelial cells at the center.

Kidneys: There was a high grade of lymphoid infiltration, both diffuse and circumscribed. A broad band of tissue in the cortex showed no trace of parenchyma, nothing but lymphoid cells, with a reticulum of fine connective tissue with capillaries. Elsewhere in the cortex there were strips of infiltration about the vessels, and parallel to the straight tubules, which were shoved widely apart. The parenchyma appeared normal.

The lungs, heart, stomach, intestine, ovary and urinary bladder all showed a moderate infiltration with lymphoid cells. The adrenal gland was normal.

The histologic picture was so typical that Dr. Mallory made the diagnosis of lymphatic leukemia without hesitation. There can be little question that this case should be classified as lymphatic leukemia of the "aleukemic" or "preleukemic" type; that is to say, without increase in the leukocyte count. The histologic appearance of the salivary glands, however, is identical with that described in many cases of Mikulicz' disease without involvement of the blood or lymphatic system, so that the case also fits in with the Mikulicz syndrome. The absence of enlargement of the lacrimal glands does not preclude such a classification, for although in the *typical* cases of Mikulicz' disease the lacrimals are involved, a number of instances have been reported in which they were not.

A search of the literature shows that the association of leukemia with the Mikulicz syndrome is extremely rare, only eight cases having or leukemia (eight out of twelve). The preponderance of females over males (eight out of twelve) may well be due to chance. Reuss[4] has reported four cases of chronic relapsing parotitis in children, in which both sides were affected, but which differed from Mikulicz' disease in that there were acute exacerbations of an inflammatory character.

MIKULICZ' DISEASE IN CHILDREN

Up to the present time twelve cases of children showing the Mikulicz syndrome have been reported. The only striking difference from the disease as seen in adults is the large proportion with pseudoleukemia or leukemia (eight out of twelve). The preponderance of females over males (eight out of twelve) may well be due to chance. Reuss[4] has reported four cases of chronic relapsing parotitis in children, in which both sides were affected, but which differed from Mikulicz' disease in that there were acute exacerbations of an inflammatory character.

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[4] Von Reuss, A.: Jahrb. f. Kinderh., 1909, lxx, 161.

CLASSIFICATION

The cases reported as Mikulicz' disease may be divided into three main groups as follows: 1. Those with involvement of the lacrimal and salivary glands in various combinations, but without changes in the blood, lymph-nodes or spleen; this is the Mikulicz' disease *par excellence*. 2. Those with enlargement of the lymph-nodes or spleen, or both. 3. Those with leukemia.

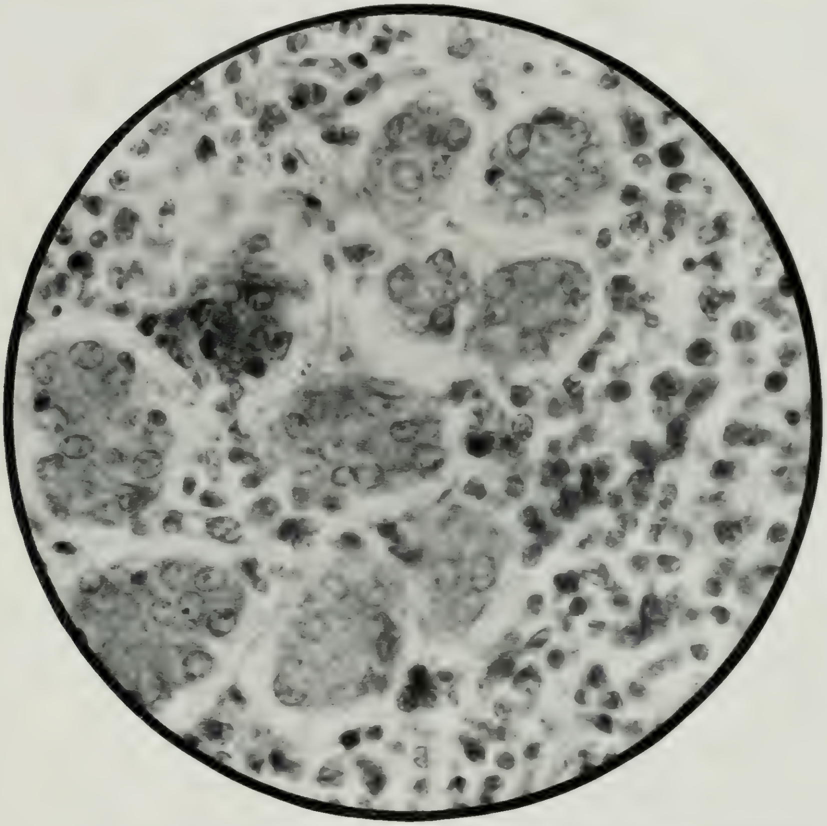

Fig. 2.—Photomicrograph of parotid gland, high power, showing acini and infiltration with lymphoid cells.

The first two groups are represented by numerous examples, while the third is a rare condition. Some of the cases in group two are probably to be considered as belonging to pseudoleukemia, especially those with very large spleens, with skin nodules, and with lymphomata in the intestine (Butterfield's case).[5]

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[5] Butterfield, E. E.: Physician and Surg., Detroit, 1907, xxix, 49.

ETIOLOGY

It is evident to anyone who studies the literature carefully that several different conditions have been described as Mikulicz' disease. Those cases showing leukemia or pseudoleukemia may be eliminated at once; they are simply unusual locations of the lymphomata common to these diseases. It should be emphasized, however, that a number of cases have been classed as pseudoleukemia without sufficient evidence; in many of them it is simply stated that the spleen and the lymph-nodes were increased in size, without mentioning the degree of the enlargement. Yet a moderate degree of enlargement of these structures is often met with in most of the chronic infectious diseases. The frequency of recovery in these cases (in Fleischer's[6] Case 1 the patient was well eight years later) is quite against the diagnosis of pseudoleukemia. One can find comparatively few out of the many cases with enlarged spleen and lymph-nodes in which the diagnosis of pseudoleukemia will bear a strict critique.

The interesting cases of simple hypertrophy of the salivary glands should also be excluded. This is a rare condition, described hitherto only by French observers. In two such cases (Jayle[7] and Frenkel[8]) tissue removed by incision showed normal structure. Apert's[9] case of dwarf growth in a man with enlargement of the parotids and breasts and glycosuria probably belongs in this class.

After these limitations there remains a considerable number of cases to which the term Mikulicz' disease may be more properly applied. They present the following features: chronic, painless and symmetrical enlargement of the salivary glands or lacrimal glands, or both, with or without moderate enlargement of the spleen and lymph-nodes; a benign course with no tendency to recurrence after complete extirpation of the affected glands; frequent cure under the use of arsenic, iodids or the *x*-ray, sometimes spontaneously.

For a part of the cases of Mikulicz' disease in this stricter sense, tuberculosis is the probable cause, as has been shown by Fleischer.[6] This observer reported four such cases, in two of which typical tubercles were found in the excised glands. The diagnosis was confirmed by Baumgarten. In one of these two the swellings of the salivary and lacrimal glands and a tuberculous iritis disappeared during a tuberculin cure. In none of the patients, however, were tubercle bacilli found in the glands. In Napp's[10] case, which was in other respects typical, miliary-

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6. Fleischer, B.: Klin. Monatsbl. f. Augenh., 1910, xlviii, 289.
7. Jayle: Bull. Soc. anat. d. Paris, 1894, 5 S. viii, 120.
8. Frenkel, H.: Arch. méd. de Toulouse, 1909, xvi, 73.
9. Apert, E.: Bull. et mém. Soc. méd. d. hôp de Paris, 1908, xxv, 155.
10. Napp, O.: Ztschr. f. Augenh., 1907, xvii, 513.

tubercles with caseation and tubercle bacilli were found in a bit of the conjunctiva which was excised. The ultimate proof, the demonstration of tubercle bacilli in the salivary or lacrimal glands themselves, still remains to be furnished, and it is possible that some cases taken to be tuberculosis were in reality instances of Hodgkin's disease of the Fischer-Reed type, which notoriously resembles tuberculosis.

Syphilis could be excluded in most cases and was the probable cause in only one, that of Gutmann,[11] in which a typical Mikulicz syndrome occurred three years after infection in a man who had previously shown the eruption of secondary syphilis; the administration of potassium iodid was followed by a cure, but no certain proof of the syphilitic nature of the Mikulicz syndrome was adduced.

For the remaining cases the etiology is obscure. The most likely cause seems to be some infectious agent in the widest sense of the word, as Mikulicz himself assumed. The possible modes of entrance are twofold; either by the ducts or by the blood current. In favor of the former are the facts that the lacrimal glands are almost always involved first, and that in many instances there has been a previous or coincident inflammation of the conjunctiva. In favor of infection by the blood current is the bilateral character of the affection.

PATHOLOGIC ANATOMY AND HISTOLOGY

The affected glands are uniformly enlarged and hard, the normal markings lost. Microscopically two types may be distinguished: (1) the lymphomatous, in which the acini are pushed apart by dense masses of cells of the lymphoid series, and (2) the chronic inflammatory, in which in addition to lymphocytes there are granulation tissue, endothelial cells, often giant cells and eosinophils. The first type is somewhat the more common; the second includes cases which may have been tuberculosis, or possibly Hodgkin's disease.

THE SYMPTOMATOLOGY

There remains little to be added to what has been said already. Besides the glands already mentioned there is frequently involvement of other glands related to the lacrimal-salivary system, such as the accessory lacrimals, Krause's glands in the upper eye-lid, the Nuhn gland on the under surface of the tip of the tongue, and sometimes the mucous glands of the mouth. There are sometimes small nodules in the conjunctiva. There may be disturbance of the function of the affected glands, usually in the form of diminished secretion, so that the mouth is dry and the shedding of tears is impossible. In many cases, however, the function has not been interfered with. The general health is not impaired, except in those cases associated with pseudoleukemia or leukemia, and symptoms of inflammation are conspicuous by their absence.

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[11] Gutmann: Berl. klin. Wchnschr., 1907, xliv, 1141.

DIFFERENTIAL DIAGNOSIS

The diagnosis of those cases showing the complete syndrome is easy. Mikulicz' disease is distinguished from *lymphosarcoma* by the more chronic course and by the (usual) absence of swelling of the regional lymph-nodes; from *primary tumors* by the fact that both sides are involved; from *pseudoleukemia* and *leukemia* by the course of the disease and the examination of the blood. From *chronic relapsing parotitis* it is differentiated by the absence of symptoms of inflammation, and from *simple hypertrophy* by the histologic appearances, and the presence of enlargement of the lacrimal glands. The fact that plumbism and iodism may occasionally cause parotid swellings should be borne in mind; also the occasional persistence for a few months of the swelling due to mumps. The *acute* Mikulicz syndrome described by Snegireff[12] only lasts a few days or weeks, and hence leads to no difficulty.

PROGNOSIS

The prognosis as to life is good in the cases not complicated with leukemia or pseudoleukemia. These latter diseases, however, can be excluded only by observation of the patient and repeated blood examinations, so that the prognosis should be guarded at first. A disappearance of the glandular swellings is likely to occur under treatment, but rarely spontaneously. During the course of acute infectious diseases a diminution of the size of the glands has been noted frequently, but it is followed by an increase to the former size.

TREATMENT

In a number of cases, the use of potassium iodid or arsenic has been followed by recovery. When these were ineffectual, exposure to the *x*-ray has in all the reported cases (Pfeiffer,[13] Haenisch,[14] Ranzi,[15] Fittig[16]) led to a disappearance of the swellings; relapses occurred in Pfeiffer's case, but were readily overcome by further *x*-ray treatment. Histologic studies by Pfeiffer showed that the *x*-ray exposures caused a disappearance of the lymphoid tissue, which was replaced by fibrous connective tissue, as occurs on exposure of *normal* lymphoid tissue to these rays.

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[12] Snegireff, K. W.: Klin. Monatsbl. f. Augenh., 1906, xliv,^{2} 245.

[13] Pfeiffer, C.: Beitr. z. klin. Chir., 1906, l, 145.

[14] Haenisch, F.: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1906-7, x, 291.

[15] Ranzi, E.: Mitt. a. d. Grenzgeb. d. med. Chir., 1906, xvi, 554.

[16] Fittig: Allg. med. Centr-Ztg., 1904, lxxiii, 606.

Complete extirpation of the glands is not followed by recurrence, but it is out of the question in the case of parotid on account of the certainty of damage to the facial nerve.

CONCLUSIONS

1. The term Mikulicz' disease should be reserved for those cases of chronic, painless bilateral enlargement of the salivary and lacrimal glands in which pseudoleukemia and leukemia can be excluded.

2. The cases occurring in the last-named diseases should be classified as pseudoleukemia or leukemia with the Mikulicz syndrome.

3. The cause of Mikulicz' disease is probably some infectious agent in the widest sense of the word. It is likely that a number of different organisms may cause the symptoms of the disease.

For the bibliography the reader is referred to a recent article by C. P. Howard.[17] This writer, however, includes some cases which hardly belong in this category; e. g., cases of simple hypertrophy of the parotid gland and cases of unilateral involvement of a single gland.

I am indebted to Prof. F. B. Mallory for valuable assistance in the histologic work.

308 Crown Street.

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Meller, J.: (Case II), Klin. Monatsbl. f. Augenh., 1906, xliv, 177.
Osler, W.: Amer. Jour. Med. Sc., 1898, cxv, 27.

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[17] Howard, C. P.: Internat. Clin., 1909, 19 S., i, 30.

A STUDY OF THE CALORIC NEEDS OF PREMATURE INFANTS

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The purpose of this paper is not to go into the details of the care and treatment of premature infants. It is rather to give such practical points and conclusions as have been arrived at after a study of the histories and development of the present series of seventeen cases, which have been selected, not because of their being ideal cases, but because they presented the different phases illustrated by proper under- and overfeeding as estimated by the caloric standard for nutritional needs as suggested by Budin, L. F. Meyer and others. The infants under discussion were fed rather according to the scale, with more especial attention to the temperature, stools, abdominal distention, cyanosis and general symptomatology, and only later their records were reviewed to ascertain the caloric intake. All except Infants 1 and 2 left the hospital in good health at the end of the period tabulated.

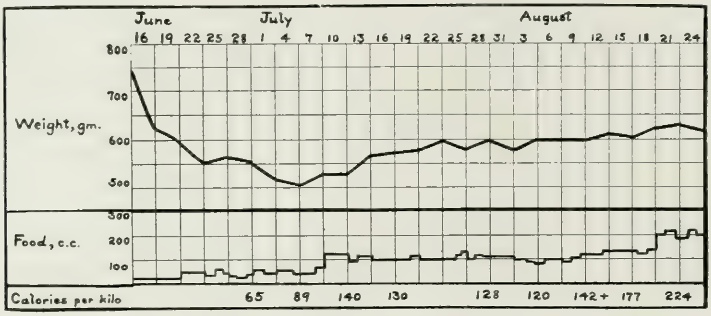
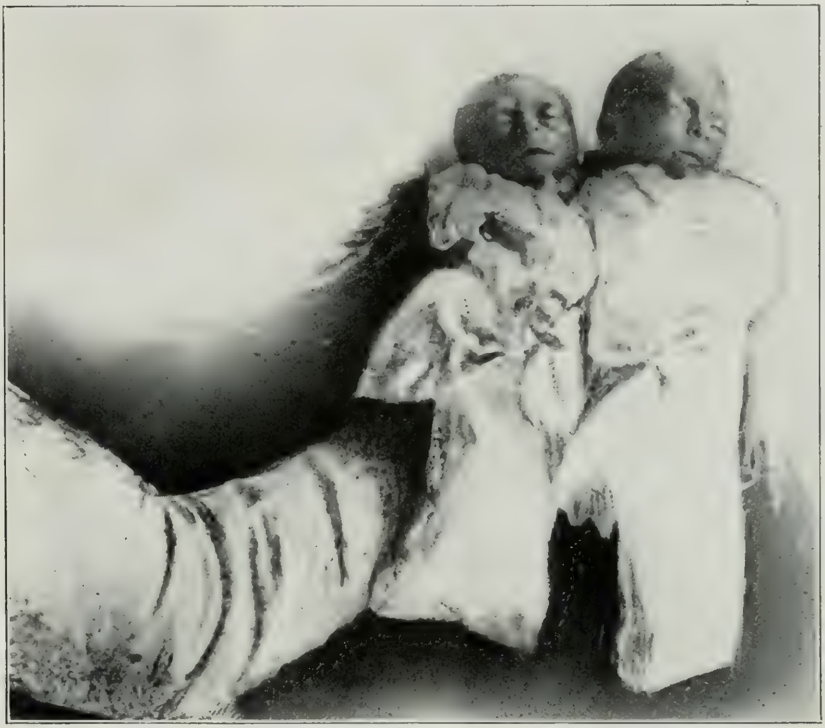


Chart 1.—Weight and food curves and calories per pound weight in Case 1. The patient entered June 16, 1916, aged 1 day; weight 740 gm.; condition bad; died Aug. 27, 1910; aged 75 days; weight 615 gm.

The infants have all been fed human milk exclusively while under my care. Those too weak to nurse have been catheter-fed or the Breck feeder has been used, while in those nursing, the milk taken has been estimated by weighing before and after feeding. The cases have been classified according to weight into those weighing under 1,000 gm., those between 1,000 and 1,500, and those over 1,500 gm.

CASES 1 AND 2.—Martha and Augusta were twins, born of a Greek family at 6½ months, and were delivered by a midwife. The mother visited the children at the hospital on the fourth day after their birth and on the following, the fifth day, gave birth to a third, still-born fetus with a second placenta, and was again out on the ninth day. No less interesting were some of the deformities in the case of Baby Martha of this interesting group of triplets. She had but two fingers on one hand, and both knees and elbows were ankylosed in extension; in fact, there seemed to be an absence of the joint surfaces; while Baby Augusta had freedom of motion in all of her joints. Considering their prematurity, 6½ months, their weight at birth, 740 and 690 gm., respectively, together with the deformities in Baby Martha, it is surprising to find them surviving to 72 and 71 days, when both succumbed during attacks of cyanosis, due in all probability to over-feeding.

Because of Baby Augusta's better development, she was fed greater quantities from the start and although she did not have as great an initial fall in weight, both continued to lose until the twentieth day, Baby Augusta losing a total of 200 gm. and Baby Martha 230 gm. in this time. The records are rather incomplete as to the food given in Case 2 during this period. In Case 1, the estimates run from 65 to 89 calories per kilo. From the twentieth day on both infants showed almost stationary weight with food values below 120 and the greatest gain on an energy quotient[1] between 130 and 140; and death in both cases with an energy quotient of over 200.



Photograph of twins, Cases 1 and 2.

CASE 3.—Baby Ethna, with a birth-weight of 1,360 gm., showed a steady increase after 137 was reached and continued to grow steadily until 220 was passed, although the growth averaged only 12 gm. daily, being lower than several infants fed with a much lower energy quotient.

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[1] Energy quotients were calculated by measuring the total quantity of human milk (in liters) fed in twenty-four hours and multiplyinig by 700 (caloric value of 1 liter of human milk) and dividing by the infant's weight (in kilograms).

CASE 4.—Baby George, birth-weight 1,335 gm., had an average daily gain of 14 gm. with an average energy quotient between 95 and 161.

CASE 5.—Baby Hattie, birth-weight 1,435 gm., showed a daily gain of 17 gm. on an energy quotient of 116 to 148.

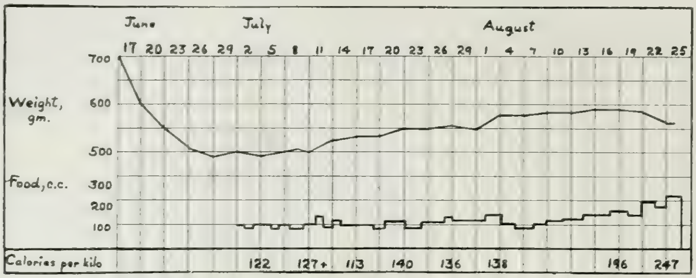

Chart 2.—Weight and food curves and calories per pound weight in Case 2. The patient entered June 17, 1910, aged 1 day; weight 690 gm.; condition bad; died Aug. 26, 1910; aged 74 days; weight 565 gm.

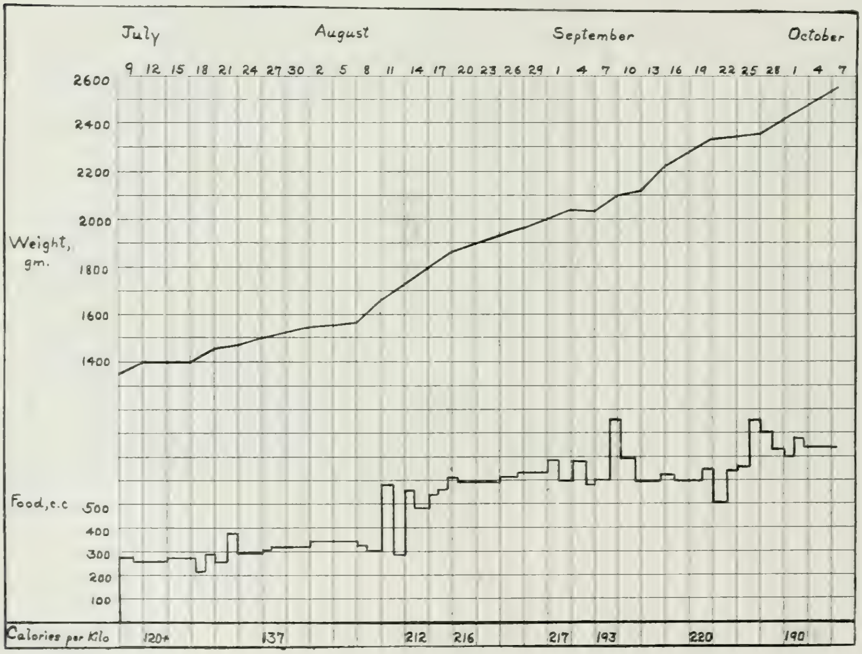

Chart 3.—Showing weight and food curves and calories per pound weight in Case 3. The patient entered the hospital, July 9, 1907, aged one day; weight 1,360 gm.; condition fair; discharged Oct. 5, 1907; aged 88 days; weight 2,512 gm.; condition good.

CASE 6.—Baby Nell-Helen, birth-weight 1,420 gm., showed an average daily gain of 27 gm. on an energy quotient of 115 to 144; the curve being more regular as the latter figure was approached.

Case 7.—Baby Juanita, birth-weight 1,070 gm., has an ideal curve with an energy quotient ranging between 132 and 170, and an average daily gain of 14 gm. over a period of ninety days.

Case 8. Baby Grace, with a birth-weight of 1,440 gm., showed initial gain on 102 calories, followed by a loss when the same was reduced below 100; followed by a gain at 100, and a steady loss at 91; a moderate gain at 109; the loss was again repeated at 90.5 and was followed by a rapid gain at 130 to 137, averaging daily 24.5 gm., and a less rapid growth, with greater fluctuations, at 115 to 109.5, averaging 10 gm. daily, and again rapidly rising with 124.

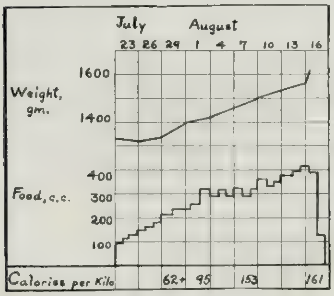

Chart 4

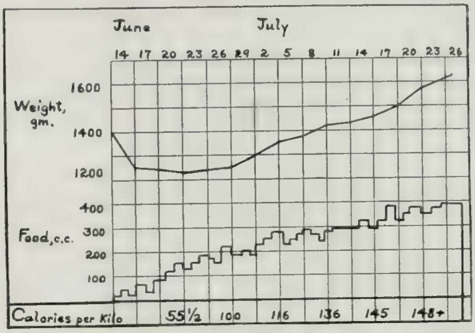

Chart 5

Chart 4.—Weight and food curves and calories per pound weight in Case 4. The patient entered July 23, 1910, aged one day; weight 1,335 gm.; condition fair; discharged Aug. 16, 1910; aged 24 days; weight 1,625 gm.; condition good.

Chart 5.—Weight and food curves and calories per pound weight in Case 5. The patient entered June 14, 1910, aged one day; weight 1,435 gm.; condition fair; discharged July 27, 1910; aged 43 days; weight 1,650 gm.; condition good.

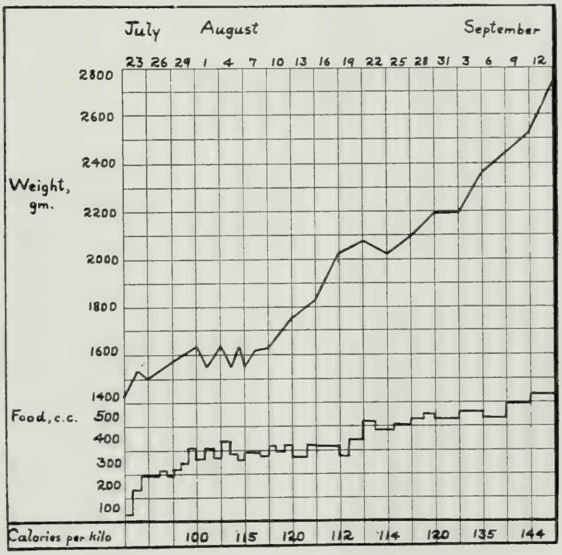

Chart 6.—Weight and food curves and calories per pound weight in Case 6. The patient entered July 23, 1907, aged one day; weight 1,420 gm.; condition fair; discharged Sept. 18, 1907; aged 57 days; weight 2,960 gm.; condition good.

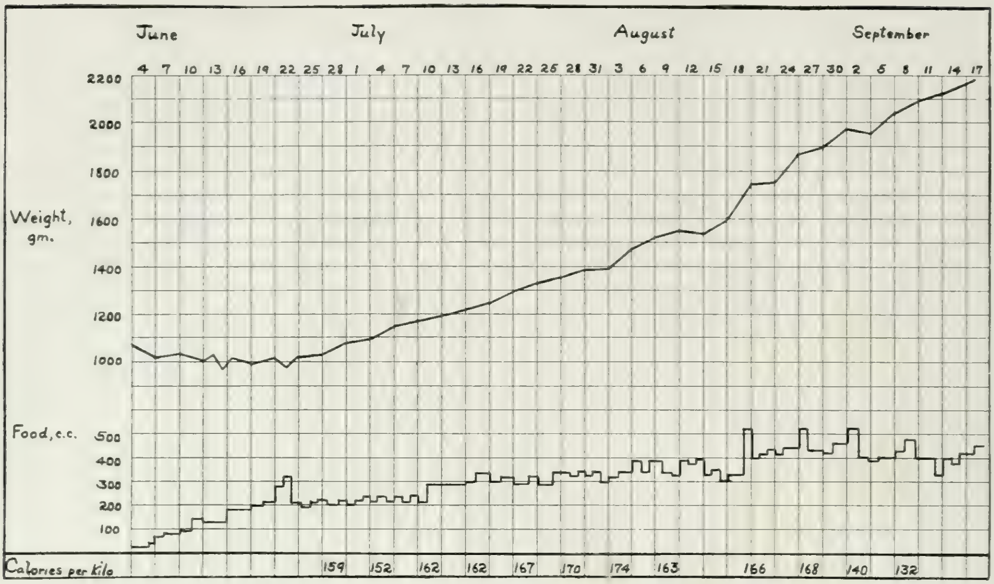

Chart 7.—Weight and food curves and calories per pound weight in Case 7. The patient entered June 4, 1910, aged one day; weight 1,070 gm.; condition fair; discharged Sept. 18, 1910; aged 105 days; weight 2,180 gm.; condition good.

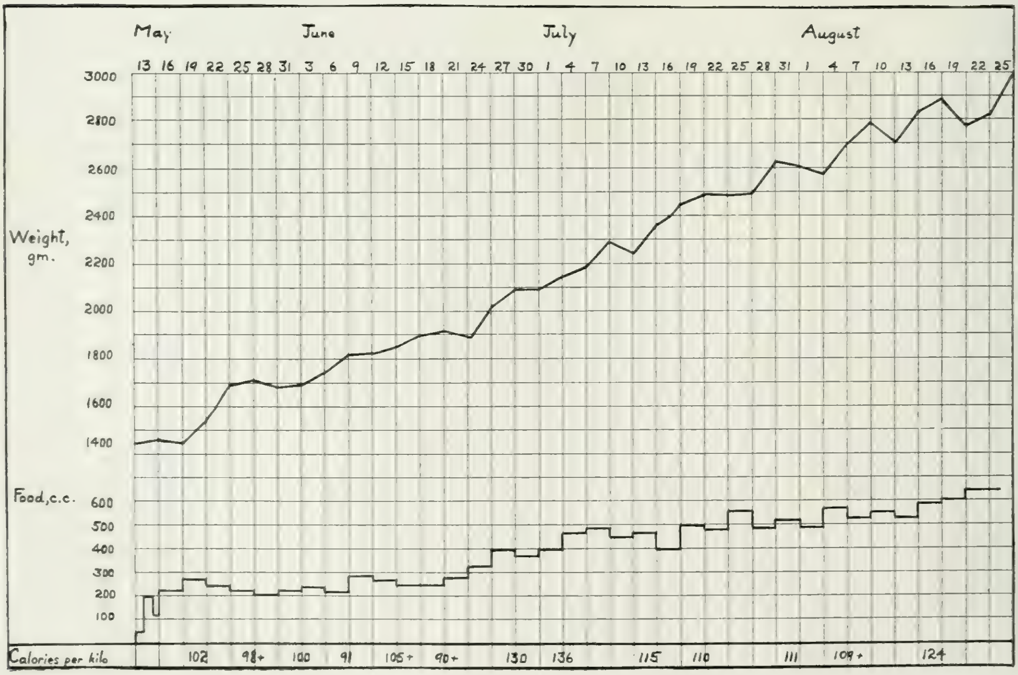

Chart 8.—Weight and food curves and calories per pound weight in Case 8. The patient entered May 13, 1907, aged 1 day; weight 1,440 gm.; condition fair; discharged Aug. 27, 1907; aged 106 days; weight 2,960 gm.; condition good.

In infants weighing between 1,500 and 2,000 gm. at birth, however, there is a more certain tendency to gain steadily at an energy quotient nearer 100. The ability of an infant to adapt itself to higher food values is beautifully illustrated in Case 9, Baby George, who gained steadily with only slight fluctuations on values gradually increased to 169.

Case 10.—Baby Stella showed the most ideal curve with an average daily gain of 37 gm., gaining 1,130 gm. in one month on an energy quotient gradually increased from 105 to 131.

Case 11.—Baby Marie first showed a gain at 104, continuing to gain on 102 and 119, but far less rapidly than Case 10, with its higher quotient, averaging only 21.5 gm. daily.

Case 12.—Baby Martin Jo had a steady gain, averaging daily 18 on an energy quotient of 127 to 170, with an average daily gain of 9.5 on an energy quotient between 170 and 206, associated with marked fluctuations and a tendency towards disturbed metabolic balance.

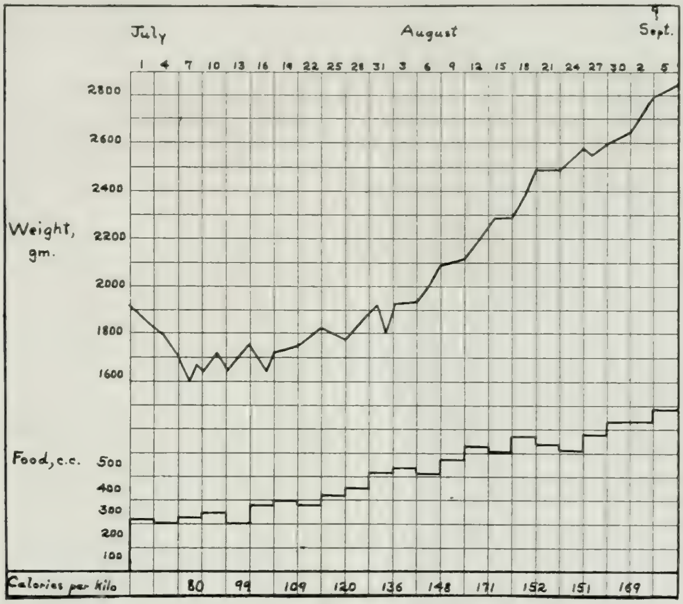

Chart 9.—Weight and food curves and calories per pound weight in Case 9. The patient entered July 1, 1907, aged 1 day; weight 1,935 gm.; condition fair; discharged Sept. 8, 1907; aged 69 days; weight 2,835 gm.; condition good.

Case 13.—Baby Jim shares with Case 10 the laurels of steady gain, and as in Case 10, the energy quotient is relatively low and the fluctuations small, averaging between 111 and 120, with an average daily gain of 40 gm.

Case 14.—Baby Mike also presented a steady curve on an energy quotient ranging from 94.5 to 118.5. He was the largest child and, as is the rule, the larger the infant the smaller the energy quotient needed for increasing weight, the average being 43 gm. gained per day.

Case 15.—Baby Marie, a smaller infant, showed her best gain at 125, with marked fluctuations in weight below 100.

Case 16.—Baby Edythe showed another steady curve with regular gain with the energy quotient between 164.5 and 120, averaging 23 gm. daily increase.

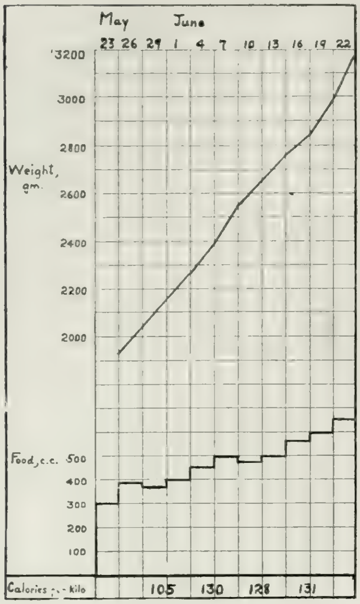

Chart 10

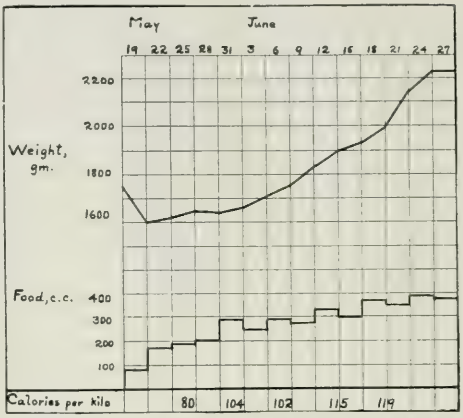

Chart 11

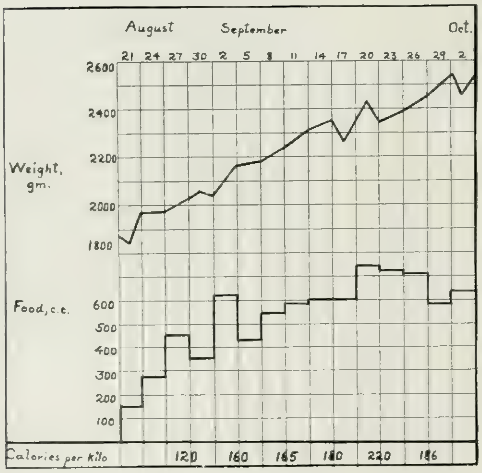

Chart 12

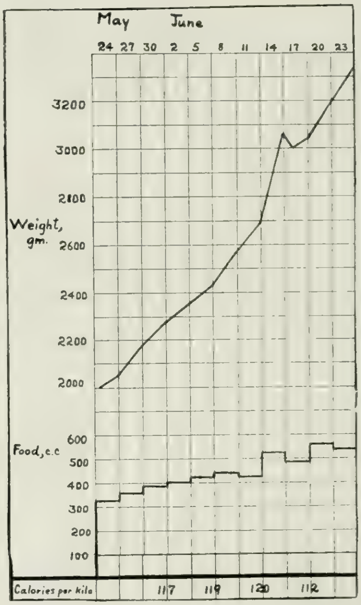

Chart 13

Chart 10.—Weight and food curves and calories per pound weight in Case 10. The patient entered May 23, 1909, aged 1 day; weight 1,930 gm.; condition fair; discharged June 22, 1909; aged 30 days; weight 3,160 gm.; condition good.

Chart 11.—Weight and food curves and calories per pound weight in Case 11. The patient entered May 19, 1910, aged 1 day; weight 1,750 gm.; condition fair; discharged June 28, 1910; aged 40 days; weight 2,225 gm.; condition good.

Chart 12.—Weight and food curves and calories per pound weight in Case 12. The patient entered Aug. 21, 1907, aged 1 day; weight 1,890 gm.; condition fair; discharged Oct. 5, 1907; aged 45 days; weight 2,515 gm.; condition good.

Chart 13.—Weight and food curves and calories per pound weight in Case 13. The patient entered May 24, 1909, aged 1 day; weight 1,950 gm.; condition fair; discharged June 26, 1909; aged 33 days; weight 3,315 gm.; condition good.

Case 17.—Baby Josephine, although one of the largest in the series, weighing 1,960 gm. at birth, showed a loss of weight at 60.5, a minimum gain at 88.5 and a rapid gain between 105 and 132, averaging 25 gm. daily.

DEDUCTIONS

1. The twins, weighing, respectively, 740 and 690 gm. at birth, showed regular gains in weight when the energy quotient averaged between 120 and 170; when 200 was passed death followed in both infants.

2. In a study of six infants with a birth-weight averaging between 1,000 and 1,500 gm., we find four infants with energy quotients fluctuating between 115 and 170, averaging daily gains between 14 and 27 gm., while those with wider fluctuation, Cases 3 and 4, gained on an average 12 to 14 gm. daily.

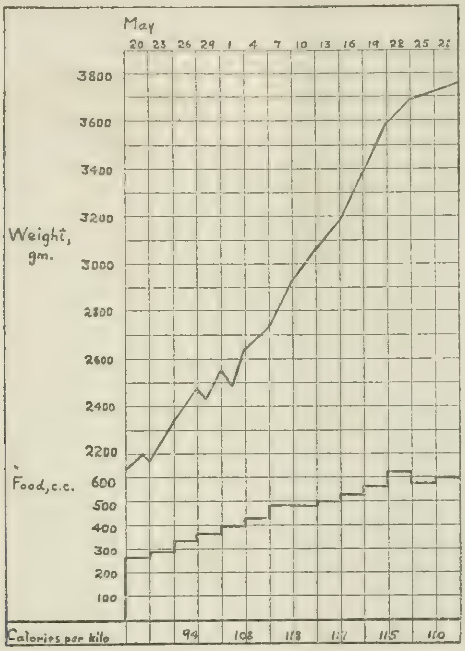

Chart 14.—Weight and food curves and calories per pound weight in Case 14. The patient entered May 20, 1909, aged 1 day; weight 2,010 gm.; condition good; discharged June 29, 1909; aged 40 days; weight 3,775 gm.; condition good.

3. Infants with birth-weights between 1,500 and 2,000 gm. showed the best results when being fed between 102 and 132. The largest infant with a birth-weight of 2,010 gm. gained on 94.5 to 118.5 apparently with equal rapidity, while Infant 12 showed marked fluctuations when an energy quotient was passed.

CONCLUSIONS

In conclusion it is safe to state that the figures of Budin and others, of an energy quotient of 100 set for the full-term new-born infant, does not hold for the premature and under-weight infant, but I would say that the energy quotient needed, varies inversely with the age and birth-weight, the energy quotient averaging between 115 and 170 in those below 1,500 gm. and 100 and 132 in those over 1,500 gm. These figures are not arbitrary, and, of all things, should not lead to an attempt to feed

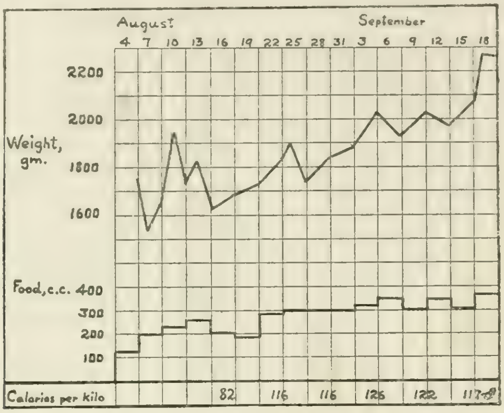

Chart 15.—Weight and food curves and calories per pound weight in Case 15. The patient entered Aug. 1, 1907, aged 1 day; weight 1,765 gm.; condition fair; discharged Sept. 18, 1907; aged 49 days; weight 2,120 gm.; condition good.

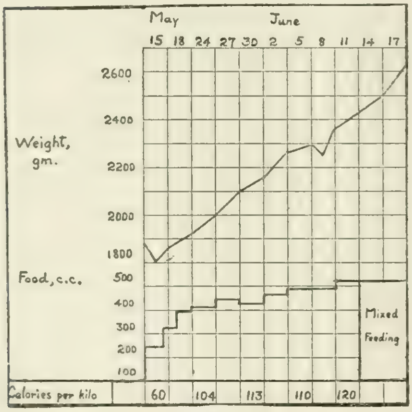

Chart 16

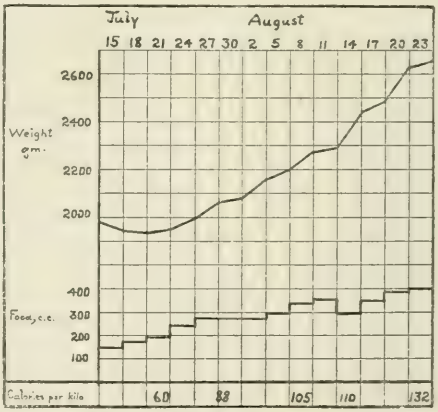

Chart 17

Chart 16.—Weight and food curves and calories per pound weight in Case 16. The patient entered May 15, 1910, aged 1 day; weight 1,875 gm.; condition fair; discharged June 16, 1910; aged 32 days; weight 2,615 gm.; condition good.

Chart 17.—Weight and food curves and calories per pound weight in Case 17. The patient entered July 15, 1907, aged 1 day; weight 1,960 gm.; condition fair; discharged Aug. 23, 1907; aged 39 days; weight 2,635 gm.; condition good.

these values in the first few days of life; otherwise a catastrophe will result. At first not only should the caloric value of the food be low, but the quantity of each feeding should also be small.

1. These infants, therefore, should be fed small quantities, frequently repeated, i.e., every one and one-half to two hours during the day and two to three hours during the night, according to the development of the individual, with special reference to the digestive organs, stools, urine and presence or absence of vomiting.

2. On the first day following the first bowel evacuation the human milk may be fed diluted with one or two parts of water or sugar, with a caloric value approximating 30.

3. From the second day on, in the absence of indigestion, the food may be increased by 10 calories daily. In the presence of digestive disorders greater care is necessary and it may be necessary for some days to hold the feeding in the neighborhood of 90, approximately the amount necessary to maintain the metabolic equilibrium.

4. After ten to fifteen days an attempt should be made to hold the figures, in the infant weighing less than 1,500 gm., to 120 to 140, and in those weighing over 1,500 gm. at between 110 and 130; but in all cases the infant itself should never be lost sight of, and more especially the stools and weight.

Budin's rule for the total twenty-four-hour quantity of milk to be given is very practical and is as follows: Feed one-fifth of the body-weight of the infant, or multiply the infant's weight by two and feed one-tenth of this amount. Budin used 650 calories to a liter of human milk as the basis for his estimation of the energy quotient, while in the figures I have given, I have figured the same as having a caloric value of 700, which would give an energy quotient of 10 higher with the latter; i. e., 130 with 650 as compared with 140 with 700 as a working basis.

5. Higher caloric needs of the premature are due to two factors — larger body surface proportionate to size and the consequent increased metabolic requirements. The early results quoted in my cases were obtained in infants raised in incubators, some of the later by the use of electric pads. It is quite necessary that all be provided with artificial heat whether from incubators, electric pads or hot water bottles, sufficient heating being used to cause the temperature to approach the normal. In incubators this ranges from 78 to 90 F. All of these methods are fraught with danger, and I have seen a temperature of 106 F. in an infant which was too close to the electric pad. The same dangers are attached to incubators.

One other important factor is a sufficient water-supply to counterbalance the rapid evaporation due to artificially heated and dried air and the excessive excreta of the first few days. As it has been my rule never

TABLE 1.—ENERGY QUOTIENT IN THE FIRST WEEKS OF AUTHOR'S CASES,* AND IN FEER'S CASE

Case	Feer's	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Birth-weight, gm.	3,615	740	690	1,360	1,335	1,435	1,420	1,070	1,440	1,935	1,930	1,750	1,890	1,950	2,010	1,765	1,875	1,960
Energy Quotient by weeks—																		
First	..	...	...	120	..	14.7	100	...	102	80	105	80	127	117	94.5	100	104.5	60.5
Second	89	...	...	...	95	55.5	115	...	98.5	99	130	104	159	119	108	100	113.5	88
Third	..	...	122	137	153	100	120.5	159	100	109	128	102+	170	120	118.5	90	110	105
Fourth	..	140	127.5	...	161	116	112.5	152	91	120	131	115	170	112	117.5	125	120	132
Fifth	..	130	113	...	...	136	114	162	109	120	...	119	206	111	115	114	...	110
Sixth	112	128	140	...	...	145	120	162	...	136.5	...	...	...	...	110	...	...	...
Seventh	...	120	136	212	...	148	135	167	130	148	...	...	...	..	...	...	...	...
Eighth	...	142.5	138	216	...	...	144	170	136	171	...	...	...	...	...	...	...	...
Ninth	97	177	196	217	...	...	...	174	137	152	...	...	...	...	...	...	...	...
Tenth	..	224	247	193	...	..	...	163	115	151	...	...	...	...	...	...	...	...
		(Died)	(Died)															
Eleventh	..	...	...	...	..	...	..	166	115	169	...	...	...	...	...	...	...	..
Twelfth	..	...	...	...	...	...	...	168	110	...	...	...	..	...	...	...	...	...
Thirteenth	..	...	...	...	...	...	...	140	111	...	...	...	...	...	...	...	...	...
Fourteenth	..	...	...	...	...	...	...	132	109.5	...	...	...	...	...	...	...	...	...
Fifteenth	..	...	...	...	...	...	...	...	124	...	...	...	...	...	...	...	...	...

*All left the hospital in good health except Cases 1 and 2.

TABLE 2.—SHOWING RAPIDITY OF INCREASE IN WEIGHT IN AUTHOR'S CASES*

Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Birth-weight, gm.	740	690	1,360	1,335	1,435	1,420	1,080	1,440	1,935	1,930	1,750	1,890	1,950	2,010	1,765	1,875	1,960
Gain by weeks, gm.—																	
First	165*	155*	40	15	185*	135	65*	200	300*	260	130*	130	175	240	50	85	25*
Second	20*	35*	75	100	15	65	15*	...	50	250	45	175	235	150	120*	190	65
Third	..	5*	45	85	75	130	20	105	125	260	100	35	300	320	155	110	150
Fourth	25	35	45	90	65	290	80	105	50	265	175	35	390	375	210	190	90
Fifth	15	5	125	..	100	25	95	150	85	...	175	90	300	375	...	150	180
Sixth	5	5	175	..	135	225	95	125	275	...	125	...	...	360	190	...	...
Seventh	10	20	75	..	..	210	65	65	140	...	...	...	...	...	...	...	...
Eighth	15	10	75		..	300	100	240	100	...	...	...	..	...	...	...	...
Ninth	5	15	125	..	.	..	100	..	...	...	..	..	...	...	...	...	...
Tenth	20	10	50	..	..		75	140	140	...	...	...	...	..	...	...	...
Eleventh	..	..	125	.	..	..	75	112	...	...	...	...	...	...	...	...	...
Twelfth	..	..	85	..	..	..	175	50	...	...	...	...	...	...	...	...	...
Thirteenth	..	.	..	..	..	.	100	40	...	...	...	...	...	...	...	...	...
Fourteenth	..	..	..	..	..	..	115	30	...	...	...	...	...	...	...	...	...
Fifteenth	..	..	..	..	..	..	120	50	...	...	...	...	...	...	...	...	...

*Loss in weight.

to start milk until after the first bowel movement, I have therefore found a frequent necessity for slight purgation with a minimum dose of castor-oil or milk of magnesia. I have endeavored to administer about one-sixth of the body-weight of water (inclusive of that contained in the milk) in twenty-four hours, and as in the smaller infants the first milk is given diluted one to four times during the first few days, it can be administered partly with the food; otherwise between feedings or per rectum. Example: An infant weighing about 1,200 gm. should receive 200 c.c. of water; should this infant receive 50 c.c. of milk, this can be diluted with 50 c.c. or more of water or sugar solution and the remainder administered either per rectum or between feedings.

TABLE 3.—SHOWING RANGE OF CALORIES AND DAILY GAIN

Cases	Range of Calories	Daily Gain gm.
1.	....	....
2.	....	....
3.	137 -220	12
4.	95 -161	14
5.	116 -148	17
6.	115 -144	27
7.	132 -170	24.
8.	130 -137	24.
	109.5-115	10
9.	90 -171	15.
10.	105 -131	37.
11.	102 -119	21.5
12.	127 -170	18.
	170 -206	9.5
13.	111 -120	40.
14.	94.5-118.5	43.*
15.	114 -125	15.
16.	104.5-120	23.
17.	105 -132	25.

*Largest baby.

6. Disturbed metabolic balance with a standstill in the weight-curve and indigestion with bad bowel movements frequently resulted when 140 calories per kilo were exceeded.

TABLE 4.—ENERGY QUOTIENT STUDIES IN THE FIRST MONTH (FROM OPPENHEIMER)

Studied by	Feer (Normal Child)	Perutz	Hähner	Frick	L. F. Meyer
Birth-weight	3,615	2,470	1,620	1,800	750
Energy quotient by months—					
First	89	101	82	...	...
Second	112	127	119	122	...
Third	97	114	119	134	147
Fourth	92	107	111	121	155
Fifth	...	95	103	111	198

All intestinal disturbances in premature infants should be treated as if they were atrophic infants (decomposition — Finkelstein), as they do not stand starvation well. I have not attempted to speak of the artificial feeding of these infants as I believe it should be discouraged in all cases in which the infant is born at thirty-six weeks or under. Artificially fed, full-term infants also require a higher food-value than the same infants at the breast, the average added requirement being 10 to 20 calories per kilo, which would also hold true in premature infants, and this adds materially to the dangers of this method of feeding. The energy quotient needed in my series of cases to maintain the metabolic equilibrium ranged quite close to 90, while in the full-term infant 70 is usually sufficient. The method of administration of food in each case varied with the vitality of the infant. In all cases of prematurity, syphilis should be thought of and in cases in which there is the slightest suspicion, the infant must not be placed directly on the breast.

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THE USE OF MALT SUGAR AND HIGH PERCENTAGES OF CASEIN IN INFANT FEEDING *

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The differences in the digestibility and availability of human and cow's milk by infants, according to Finkelstein and Meyer,[1] are not due to qualitative differences in the constituents of the milk. Casein causes no disturbances of digestion. Fat and sugar have no pathologic action unless the intestinal functions have been injured. The fat and sugar of human milk can act in the same way if the injury to the intestine is severe enough. The action of the whey from human and from cow's milk is, however, different. A baby can digest the various food elements when they are in human whey but cannot when they are in the whey of cow's milk. Any other medium than human milk interferes with the functionating of the intestinal epithelium. They have, however, in spite of many experiments, been unable to find a better menstruum than the whey of cow's milk.

They believe that the diarrheal diseases of infancy originate in a functional weakness of the intestine, and that this functional weakness is kept up and increased by fermentation. This being so, the first step in treatment is to stop the fermentation and in this way give the intestine an opportunity to repair itself. This has been done in the past by cutting down the amount of food and by giving foods insusceptible to fermentation. This method is sufficient in many cases; in others, however, fermentation continues even when the caloric needs are not covered. In such cases the only recourse in the past has been human milk.

Fat, sugar and protein are all susceptible to decomposition. The medium in which they are contained, that is, the whey, may also play a part in the decomposition. Czerny and others have attributed the chief rôle in fermentation to fat, but Finkelstein and Meyer conclude from their experiments, in which they obtained the same results in these cases with diluted whole milk as they did with diluted skimmed milk and buttermilk, that the fermentation is not due to fat. They also found that the addition of freshly prepared casein to skimmed milk and to dilutions of whole milk, which babies with indigestion were taking, not only did not make the babies worse but apparently improved them. The

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*Read at the meeting of the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

[1] Finkelstein and Meyer: Jahrb. f. Kinderh., 1910, lxxi, 525 and 683; Berl. klin. Wchnschr., 1910, lvii, 1165; München. med. Wchnschr., 1911, lviii, 340.

thin, acid, green stools changed in a few days to typical light-colored and dry soap-stools. They conclude, therefore, that casein has an antifermentative action and is harmless. Milk-sugar must, therefore, by exclusion, be the cause of the fermentation. They found that the addition of milk-sugar to the food of babies whose diarrhea was controlled by the addition of casein, resulted in the recurrence of the abnormal stools. The long-continued diminution of the carbohydrates in the food also relieved the symptoms, even if the casein was not increased. They adduce as further evidence that the primary cause of fermentation lies in the sugars and not in the fats, the fact that when babies having fatty diarrhea were given the same amounts of casein and fat in various saline, sugar-free solutions instead of in the sugar-holding whey, the fatty diarrhea ceased. Milk diluted with water was, moreover, better borne than milk diluted with whey.

They sum up as follows: Sugar is the special and primary cause of fermentation. Neither normal nor abnormal acidification can take place without it. The fat is never involved primarily. It is injurious in that it causes an acid fermentation. The fermentation of the sugar is dependent on two main factors—first, the concentration of the whey, more or less work being thrown on the intestinal epithelium according to whether the concentration is more or less suitable for the intestine; second, the relative proportions of casein and sugar in the mixture. Here, therefore, as always in matters of nutrition, when considering the chemistry of the intestine, it must be remembered that it is impossible to judge of the action of one element alone, and that the final result depends on the relative proportions of the various organic and inorganic elements of the food.

They conclude, therefore, that the principles on which the preparation of a food to combat intestinal fermentation depend are: a diminution in the quantity of milk sugar, a diminution of the salts through dilution of the whey and an increase in the casein, with varying, and, under certain circumstances, not inconsiderable amounts of fat. After improvement has begun an easily assimilable and consequently little fermentable carbohydrate should be added. They consequently developed a food to meet these indications, to which they gave the name of "Eiweissmilch." This food is prepared as follows:

> Heat one quart of whole milk to 100 F. Add four teaspoonfuls of essence of pepsin and stir. Let the mixture stand at 100 F. until the curd has formed. Put the mass in a linen cloth and strain off the whey from the curd. Remove the curd from the linen cloth and press it through a rather fine sieve two or three times by means of a wooden mallet or spoon. Add one pint of water to the curd during this process. The mixture should now look like milk and the precipitate must be *very finely* divided. Add 1 pint of buttermilk to this mixture.

Finkelstein and Meyer use buttermilk in the preparation of this food for the following reasons: (1) because of the small amount of milk sugar which it contains; (2) to obtain the good effects of the lactic acid, and (3) because buttermilk can be kept for a long time.

The composition of this food is:

Fats	2.5 per cent.
Sugar	1.5 per cent.
Proteid	3.0 per cent.
Salts	0.5 per cent.

One quart of this milk contains about 370 calories.

They used this food in a great variety of conditions accompanied by diarrhea, such as dyspepsia, decomposition, intoxication and parenteral infections, and in their original paper claimed good results in all, but not in the new-born.

The general principles laid down by them for the use of this food in these conditions are as follows: A preliminary catharsis, if necessary, followed or not by an initial period of starvation and tea diet, as the case may be; small amounts of casein milk; larger amounts of casein milk; the addition of some carbohydrate other than milk-sugar or cane-sugar, preferably some dextrinized preparation of malt-sugar. They claim that the loose, green stools are quickly replaced by typical soap-stools and that the addition of malt-sugar does not cause a recurrence of the symptoms of fermentation. They call attention to the fact that on account of the low nutritive value of the food there is certain to be a loss of weight in the beginning of the treatment. This is followed by a stationary period, then, when the amount of food is increased and carbohydrates added, by an increase in weight. They found that babies could be kept on this food for months and continue to thrive.

Birk[2] obtained good results in the great majority of thirty cases of various sorts in which the patients were treated with casein milk. He believes that it is unquestionably of great service in many cases; that it is indicated not only in the acute toxicoses, but also in chronic disturbances of nutrition, in so far as there is in these cases an intolerance against fat; that is, in the cases in which buttermilk is ordinarily given. He found that as the result of the diminution of the sugar and the consequent diminution of the fermentation in the intestine the tolerance of the intestine toward fat increased.

Reuss and Sperk[3] also obtained favorable results in a small number of cases. They, however, attribute a part of the favorable results to the action of bacteria, believing that the administration of large amounts of casein diminishes fermentation and acts as the provocator of large amounts of alkaline intestinal secretion which neutralizes acid products and favors the development of bacteria antagonistic to fermentation.

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[2] Birk: Monatschr. f. Kinderh., 1910, ix, 140.

[3] Reuss and Sperk: Wien. klin. Wchnschr., 1910, xxiii, 9.

Welde[4] used it in sixty cases of various types and obtained satisfactory results. Nothmann[5] also obtained good results in a few cases, but Rommel[6] and Ibrahim[7] did not have as favorable results.

Braumüller[8] also used the casein milk in fourteen cases. He found, however, that in three of his cases serious symptoms developed when sugar was added to the mixture. In these cases the addition of even small amounts of sugar was enough to bring on a slow but uncontrollable decline, of which there had previously been no warning signs. A possible explanation is that the infant's powers of assimilation are greatly weakened and that it can produce only a limited amount of ferments. The large amounts of casein and fat in the casein milk demand so much of this power that the organism has but little strength left to produce the ferments which are needed to take care of the sugar. Pawlow has shown, moreover, that the sudden withdrawal of sugar produces an extinction of the secretion of the ferments concerned. Braumüller consequently advises delay in the addition of sugar in the severer cases and the substitution of oat starch for sugar in the beginning.

Finkelstein and Meyer[1] state in a later paper that this method of treatment is worthy of employment in the disturbances of nutrition in infants which are accompanied by diarrhea, no matter of what sort or severity. In their latest paper on "The Technique and Indications for Feeding with Eiweissmilch" they are evidently endeavoring to meet criticisms which have been made of their method of feeding. In this paper they still claim perfect results, and say that the bad results obtained by others are due to imperfect technic or to a bad choice of cases. They now, however, warn especially against the continuance of under-feeding, advising the administration of as much as from 180 to 200 calories per kilo. They also warn against too long delay in the addition of carbohydrates, especially in feeble children, and against giving up treatment, withdrawing the carbohydrates and diminishing the quantity of food, if symptoms recur. They claim, too, that casein milk must not be combined with any other mixture, not even with human milk.

Leopold[9] has recently summed up the teaching of Finkelstein and his school as to the disturbances of nutrition caused by sugar in the food. These are of three sorts. It is, according to them, the chief cause of fermentation and consequently of diarrhea, plays an important part in the retention of water and, consequently, in the weight, and may cause an increase in the temperature, the so-called "sugar-fever."

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[4] Welde: Therap. Monatsh., 1911, xxv, 83.

[5] Nothmann: Jahrb. f. Kinderh., 1910, lxxii, 347.

[6] Rommel: Jahrb. f. Kinderh., 1910, lxxii, 347.

[7] Ibrahim: Jahrb. f. Kinderh., 1910, lxxii, 347.

[8] Braumüller: München. med. Wchnschr., 1910, lvii, 2571.

[9] Leopold: Ztschr. f. Kinderh., 1910, i, 217.

He also investigated the action of the different forms of sugar, given by the mouth, in relation to the causation of diarrhea, to weight and to temperature. He studied chemically-pure lactose, saccharose, maltose and glucose, Soxhlet's Nährzucker and Löflund's Nährmaltose. The analyses of Soxhlet's Nährzucker and Löflund's Nährmaltose are as follows:

		Per cent.
Soxhlet's Nährzucker =	maltose	52.44
	dextrin	41.26
	sodium chlorid	2.00
Löflund's Nährmaltose =	maltose	40.00
	dextrin	60.00
	salts	.30

Milk sugar caused diarrhea the most easily, probably on account of its relatively slow absorbability, while the dextrin-maltose mixtures were comparatively well borne. The retention of water with the various sugars depended chiefly on whether the sugar caused diarrhea or not. In some cases, however, there was a retention of water in spite of the diarrhea. Fever occurred much less frequently with the dextrin-maltose mixtures than with the pure sugars. The tendency to increase in temperature stood in close relation to the action of the given sugar in causing diarrhea. Fever never occurred in patients whose stools remained normal, proving that there must be a lesion of the intestine before fever occurs. When sugar was added to different foods, fever occurred less often with foods poor in whey than with those rich in whey.

He concludes that when a single dose of from 10 to 30 gm. of the different forms of sugar ordinarily used in feeding babies is given, the dextrin-maltose mixtures produce diarrhea and fever less easily than the pure sugars. Milk-sugar seems to be the one of the pure sugars which causes diarrhea and fever most easily. The condition of the intestine and the character of its contents, as well as the salts and sugar, are of significance in the etiology of "sugar fever." The temperature reaction occurs more frequently when the food is rich in whey than when it is poor in whey.

Having seen the rise and fall of many much-heralded foods and routine methods of feeding in the past, and being a firm believer in the adaptation of the food to the individual infant, I was not prepared to accept Finkelstein and Meyer's statements that this method of treatment is worthy of employment in all the disturbances of nutrition in infants which are accompanied by diarrhea, no matter of what sort or severity, and that all the bad results obtained by others are due to imperfect technic or to the bad choice of cases. Neither was I prepared to believe that all these disturbances occur independently of bacterial action, as the authors seem to imply. It did seem to me, however, that they had made out a very strong case against sugar as the etiologic factor in fermentation, and that the treatment of fermentative conditions with a food low in sugar and high in proteins was, therefore, a rational one. The substitution of the dextrin-maltose mixtures for lactose also seemed rational. It did not seem rational, on the other hand, to treat all cases in the same way, or to give all babies the same food without regard to their individual digestive capacities. The reasons given for the addition of buttermilk to the food, viz., its low salt content, its resistance to decomposition and its lactic acid content, did not seem very satisfactory, moreover, because the amount of salts in the precipitated casein is low, as it is in buttermilk, there is no reason for keeping the food a long time, and no evident reason why lactic acid should be of use in intestinal fermentation.

It seemed to me, however, that it would be possible to take advantage of the main principles of this method of treatment of the intestinal fermentative conditions and at the same time avoid the disadvantages of a routine food and the apparently superfluous buttermilk by applying them in the modification of milk by the percentage method. I was enabled to do this through the courtesy of the Walker-Gordon Laboratory. It was possible, by the use of cream containing a high percentage of fat, to reduce the amount of unprecipitated casein and whey proteins to a very small percentage. Any percentage of proteins desired could then be added in the form of precipitated casein. The precipitated casein was prepared according to Finkelstein and Meyer's method, the casein from one quart of milk being made into an emulsion with sufficient water to make one pint. This emulsion, according to the analysis made at the Walker-Gordon Laboratory, contained less than 0.50 per cent. of sugar. It was thus possible to get mixtures containing 3 per cent., or even more, of fat, with less than 1 per cent. of milk-sugar. The "maltose" used in the mixtures contained 88 per cent. of carbohydrates, 57.1 per cent. being in the form of maltose and 30.9 per cent. in the form of dextrin. It contained no starch and had no diastatic action. Since the percentages of the different ingredients in the mixtures were known, it was always possible to calculate the number of calories taken.

This method of treatment was tried only in cases of intestinal disturbance associated with evidences of fermentation, and in which there was none or, at most, very little vomiting. Owing to the time of year at which this study was undertaken, only sixteen suitable cases were available. Eight of these cases must be excluded because of the short duration of the trial, the use of breast-milk in addition, or the presence of associated diseases, leaving only eight for analysis. The general impression derived from the few cases of parenteral infections was that this method of treatment was not very useful in these conditions. Eight cases is, of course, too small a number to justify any sweeping conclusions. They were carefully studied, however, and seem to show, or at any rate to illustrate, certain points fairly definitely. A detailed account of some

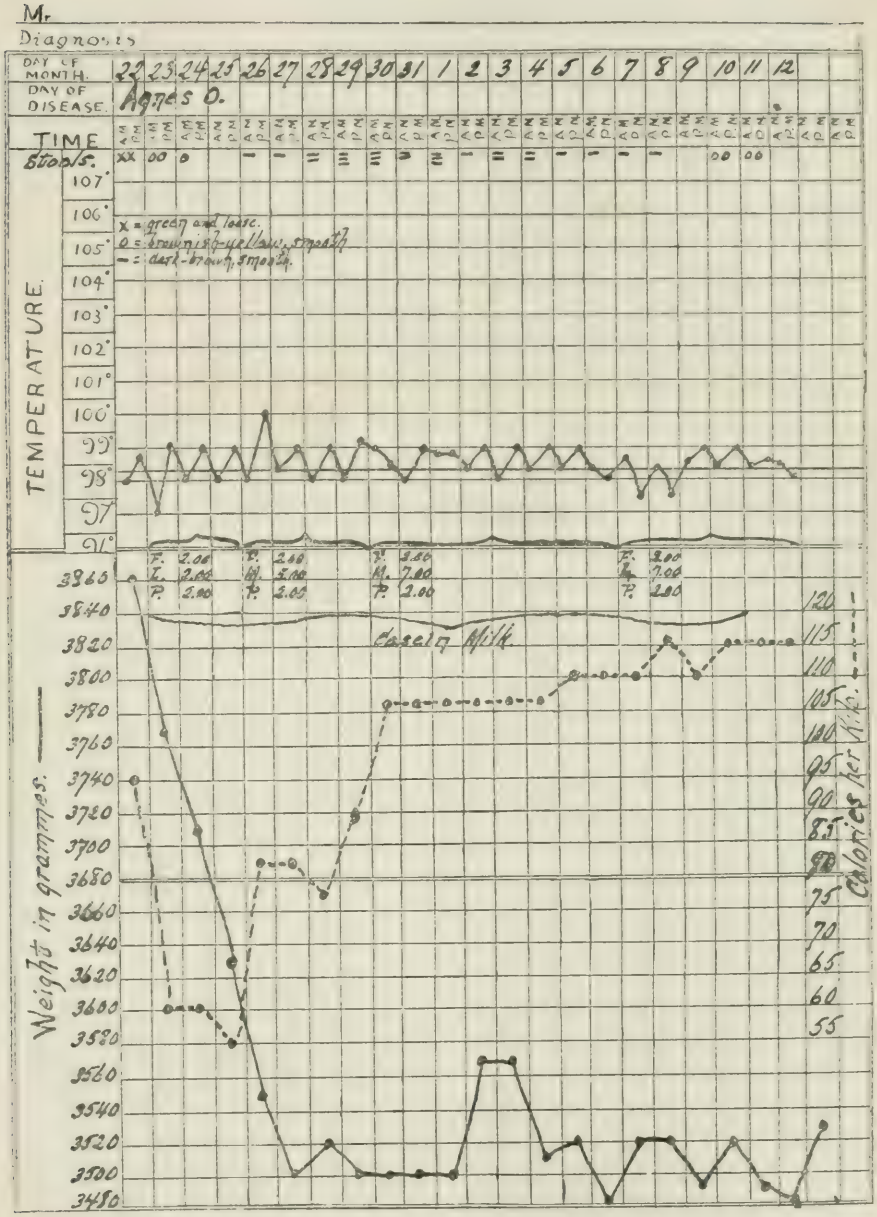

Chart 1.—Results of the use of malt sugar and high percentages of casein in Case 1.

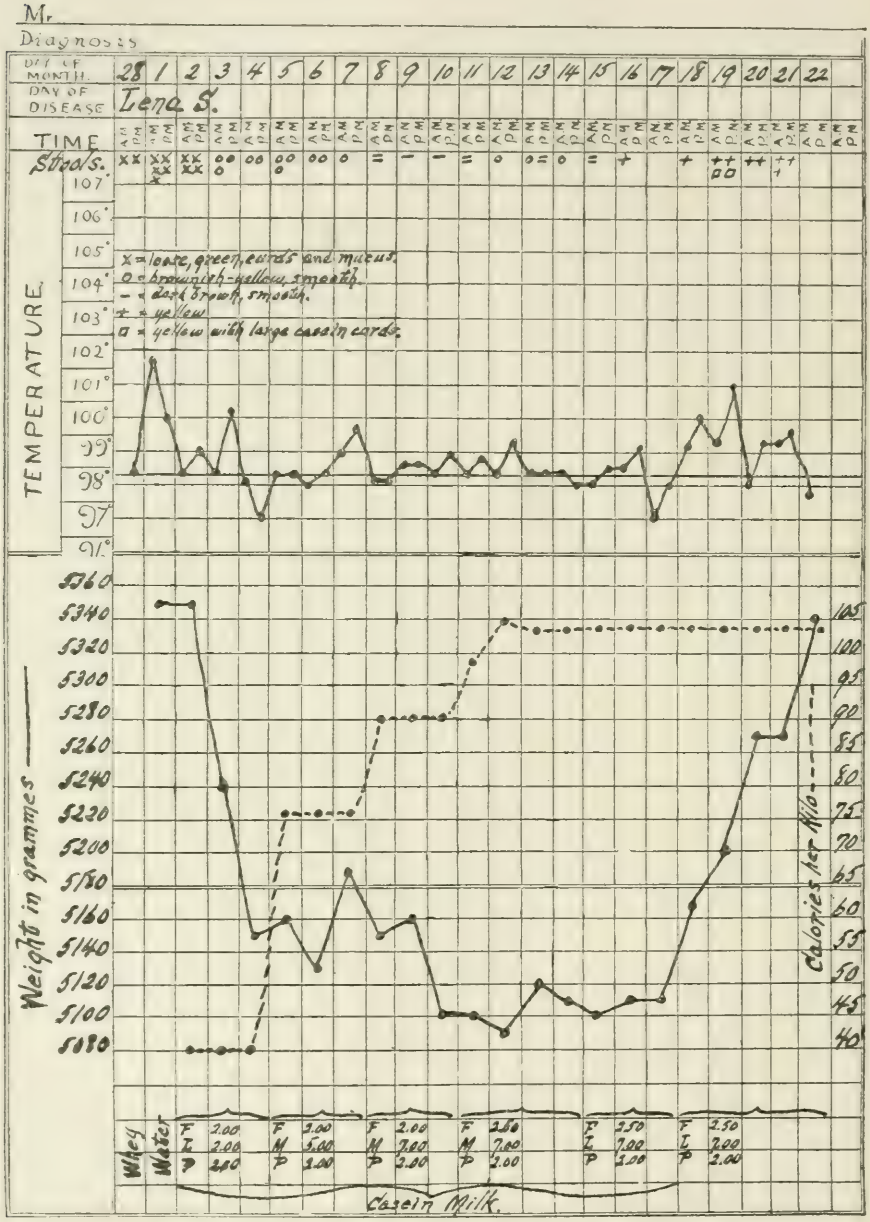

Chart 2.—Results of feeding malt sugar and high percentages of casein in Case 2.

of these cases or of parts of them will, therefore, be more instructive than any collective analysis.

CASE REPORTS

CASE 1.—A. O., 7 weeks old, was nursed for two weeks, after which she was fed on some milk mixture of unknown composition. She was brought to the Infants' Hospital by a woman who knew nothing as to the condition of her digestion or the character and number of her stools. She was in good general condition and the physical examination showed nothing abnormal. She was given a mixture containing 2 per cent. of fat, 7 per cent. of lactose, 0.75 per cent. of whey proteins and 0.25 per cent. of casein. She took this well and did not vomit, but had two large, loose, light-green stools daily.

March 23, two days after entrance, she was put on eight feedings of 75 c.c. each of a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. The stool the next day was brownish-yellow, smooth and soft. This mixture gave only 60 c. per kilo, and the weight dropped from 60 to 80 gm. daily.

The food was increased March 26 to 80 c.c. at a feeding, and maltose enough added to raise the sugars to 5 per cent. She then got a little more than 80 C. per kilo and the loss of weight ceased. The stools at once became dark brown and pasty, but contained a large amount of fat in the form of soap.

Two per cent. more of maltose was added March 29, bringing the percentage of sugar to 7, giving 100 or more C. per kilo. On this she continued to have from one to three brown and pasty stools daily, and just about held her weight.

The maltose was changed to lactose April 7, the percentage of sugar being kept at 7. The color of the stools changed to yellowish-brown but no signs of fermentation developed. The precipitated casein was replaced by ordinary milk proteins April 11 without any change in the general condition or stools (Chart 1).

In this instance the green color of the stools ceased at once when the percentage of lactose was reduced to 2 and that of the casein increased to 2. It did not recur when the percentage of sugar was increased to 7 by the addition of maltose. The tendency to fermentation was apparently relieved by this treatment, as the green color did not return when the maltose was replaced by lactose. It illustrates the loss of weight which takes place at first when the percentage of sugar is cut down. It is noticeable, however, that the baby did not gain when it was taking 100 or more calories per kilo.

CASE 2.—L. S., 4 months old, had been fed on a mixture containing 2.50 per cent. of fat, 6 per cent. of sugar and 1 per cent. of proteins and had done well until February 24, when she began to have four or five loose, green stools daily. She was admitted to the Infants' Hospital February 28. Physical examination showed nothing abnormal except the signs of slight malnutrition. She was given whey the first twenty-four hours and continued to have stools of the same character. March 1 she was given 2 teaspoonfuls of castor-oil and put on water for twenty-four hours.

March 2 she was put on a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. The stools rapidly changed in character, that passed during the afternoon of March 3 being light yellowish-brown and smooth, with a little mucus but no curds. It contained no neutral fat or fatty acids, but a moderate amount of soap. She lost a little weight.

March 5 enough maltose was added to raise the percentage of sugar to 5. The stools then became somewhat more brown and were macroscopically perfectly digested. Two per cent. more of maltose was added March 8, and March 11 the percentage of fat was increased to 2.50. While taking this mixture she had from one to three smooth, dark-brown stools daily. They contained only a small amount of soap.

Lactose was substituted for maltose March 15, the percentage of sugar being kept at 7. The green stools did not recur after the change. The precipitated casein was replaced by ordinary milk proteins March 18. The stools then began to show an occasional casein curd but contained no fat, either macroscopically or microscopically. Gain in weight began at this time, whereas the weight had been stationary on the maltose and casein milk mixture of the same caloric value (Chart 2).

In this instance also the green color of the stools ceased at once when the lactose was reduced to 2 per cent., and did not return when the percentage of sugar was increased to 7 by the addition of maltose. The tendency to fermentation was apparently relieved by the treatment, as the green color did not return when the maltose was replaced by lactose. The power of assimilating fat increased while on the maltose and casein milk mixture. It is noteworthy that casein curds appeared in the stools when ordinary milk proteins were substituted for the precipitated casein, suggesting that the casein is more easily digested after it has been precipitated and finely divided by rubbing through a sieve than when it has not been treated in this way.

Case 3.—W. C., aged 5 months, was born one month before he was expected, but weighed 7½ pounds. He was never nursed, but was fed on a great variety of proprietary foods. He did well, nevertheless, for the first three months. Since then he had been constipated, but the stools had been green and undigested. He had lost weight steadily. He was small and poorly nourished, weighing on admission to the Infants' Hospital only 3,250 gm. The physical examination showed nothing abnormal except the signs of malnutrition. A skin tuberculin test was negative. The urine was normal.

He was given a teaspoonful of castor-oil at entrance and put on barley-water, containing 0.75 per cent. of starch, for twenty-four hours. He was then given a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. He lost weight rapidly on this mixture and the stools continued to contain a few fine, soft curds. Microscopically, however, the stools contained but little fat, this being in the form of soap.

Four days later the percentage of sugar was increased to five by the addition of maltose. He continued on this mixture until his death, two weeks later. He lost weight more rapidly when the caloric value of his food was over 115 C. per kilo than when it was at about this level. The stools contained no fat, except that there were occasionally a few fine, soft curds (Chart 3).

In this instance there was but little evidence of fermentation. The stools were perfectly normal after beginning the mixture of maltose and precipitated casein and the fat was well utilized. He nevertheless failed steadily and died. He was willing to take all the food given him, but an increase in the caloric value of the food hastened rather than retarded the loss of weight (paradoxical reaction). In most instances, however,

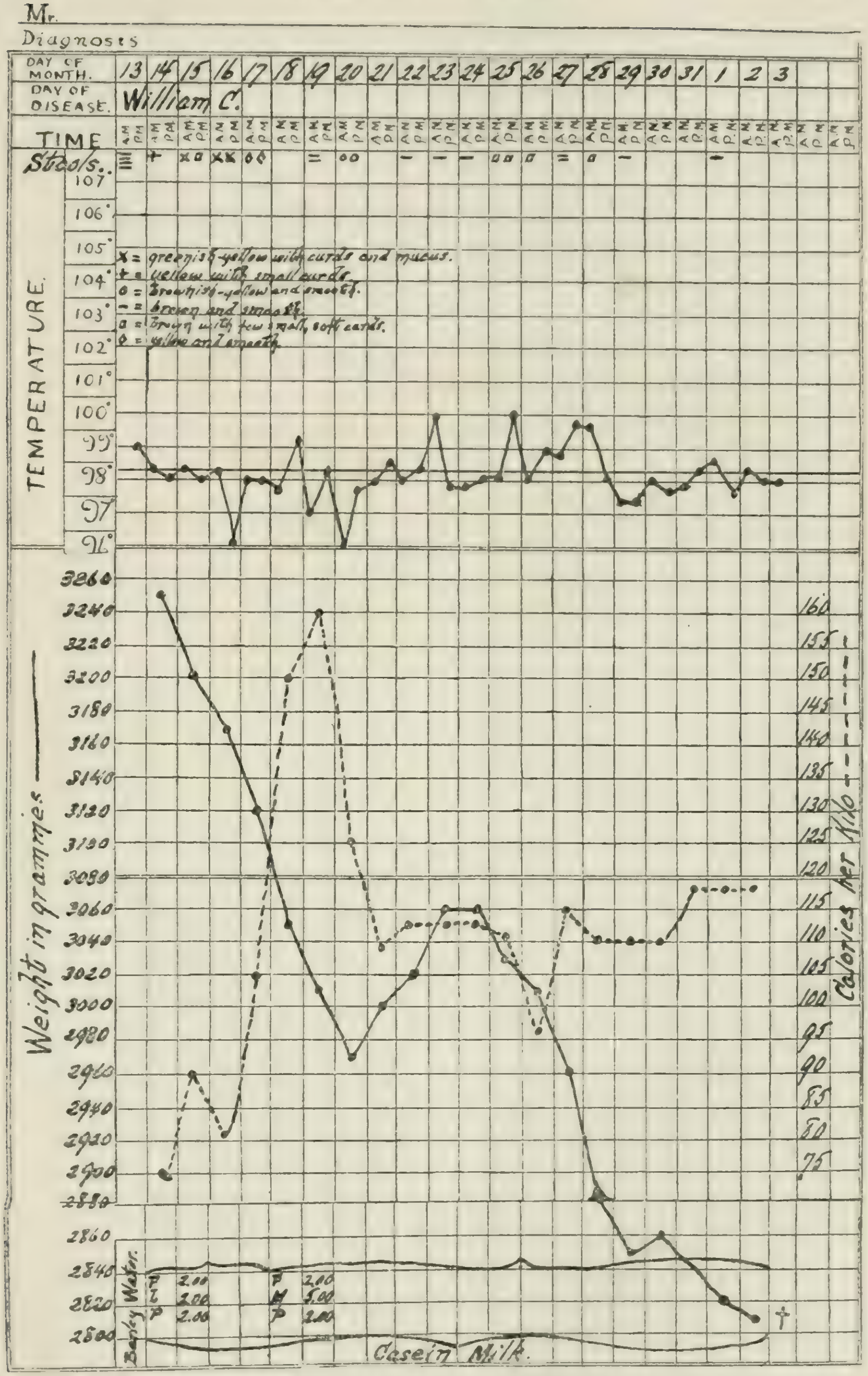

Chart 3.—Results of feeding malt sugar and high percentages of casein in Case 3.

it was impossible to get the babies to take more than 120 calories per kilo; if they did the digestion was at once disturbed. Judging from my experience with these cases it would seem very difficult to give babies from 180 to 200 C. per kilo of "casein milk," as recommended by Finkelstein and Meyer.

Case 4.—H. C., aged 4 months, had been fed for the last two months on a mixture containing 2.50 per cent. of fat, 6 per cent. of lactose and 1.50 per cent. of proteins. She had been having daily for some weeks five or six green or greenish-yellow stools, containing some curds. Physical examination showed nothing abnormal except the signs of slight malnutrition.

She was given on admission to the Infants' Hospital, April 6, a mixture containing 1 per cent. of fat, 7 per cent. of lactose, 0.90 per cent. of whey proteins and 0.25 per cent. of casein. While taking this mixture her stools were nearly normal. Thirty-six hours later it was changed, because of its low caloric value, to a mixture containing 2 per cent. of fat, 7 per cent. of lactose, 0.90 per cent. of whey proteins and 0.50 per cent. of casein. She immediately began to have numerous green or greenish-yellow, undigested stools.

Two days later she was given a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. The green color of the stools ceased at once, but the small curds and mucus persisted.

Three days later the percentage of sugar was increased to 5 by the addition of maltose. The stools became normal after a few days, although, in spite of a sufficient intake of calories, there was a progressive loss of weight.

The mixture was then changed to one containing 3 per cent. of fat, 6 per cent. of lactose and 1.50 per cent. of ordinary milk proteins. The movements continued good and the baby began to gain in weight at once, although the caloric value of the food was no higher (Chart 4).

The good effect of this method of treatment on the fermentation was evident in this instance also, but the failure to gain in weight, although the number of calories was sufficient, was also evident.

In two instances it was impossible to increase the percentage of maltose above 5 without causing vomiting. The symptoms of fermentation were relieved in these cases as in the others, but the same difficulty was experienced in making the babies gain weight. This difficulty was encountered in almost every instance, although the number of calories given was theoretically sufficient. A number of them began to gain at once, moreover, after they were changed over to ordinary mixtures, although the number of calories taken was not increased. No difficulty was encountered in changing from the maltose and precipitated casein mixtures after the symptoms of fermentation were relieved, although the stools were sometimes temporarily not as well digested.

I feel certain from my study of these few cases that this method of treatment of intestinal disturbances associated with fermentation in infancy, by the withdrawal of lactose and by raising the percentage of casein, followed by the addition of dextrin-maltose, is a most valuable one. I am inclined to think that the finely divided precipitated casein, freed from the whey proteins, has some advantages over the natural

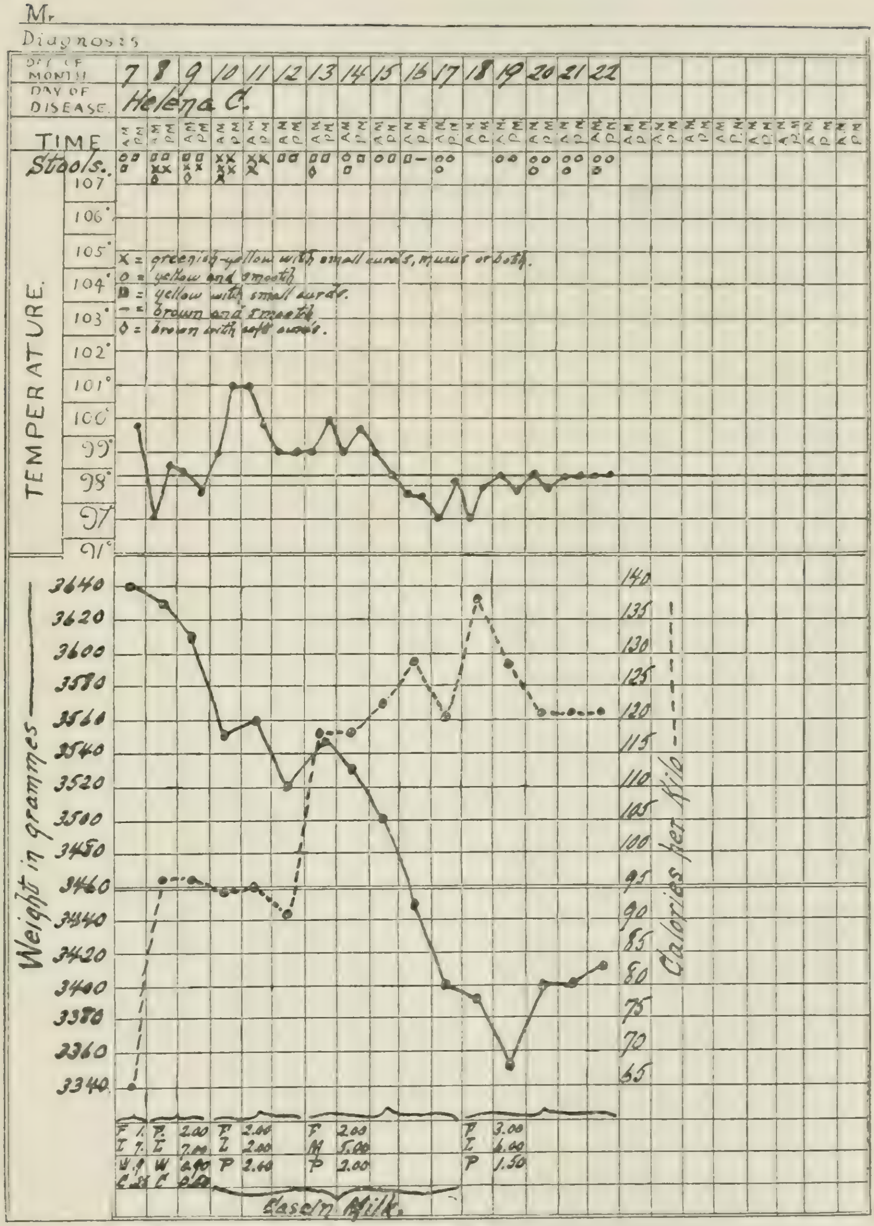

Chart 4.—Results of feeding malt sugar and high percentages of casein in Case 4.

milk proteins, but I am not sure of this point. I am also inclined to think that after the symptoms of fermentation are relieved babies do not thrive as well on these mixtures as on ordinary mixtures, and consequently believe that they should be discontinued as soon as these symptoms are relieved. I also believe, on account of the failure of babies to gain on these malt sugar and precipitated casein mixtures, even when given in amounts amply sufficient to cover the caloric needs, that this method of feeding is not one generally applicable.

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A NOTE ON THE BACTERIOLOGIC EXAMINATION OF LYMPHATIC GLANDS IN SCARLET FEVER*

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Considerable interest was recently aroused by the report of Vipond[1] regarding the specific organism of scarlet fever. The author claims to have secured a rapidly-growing spore-forming bacillus from the lymphatic glands of seven consecutive patients with scarlet fever. The injection of broth cultures of this organism is reported as having produced scarlet-fever in five monkeys and two rabbits; that the same bacilli were secured from the lymph-glands of these animals, and further, that another monkey and a rabbit contracted the disease by contact with these animals. In other words, the postulates of Koch were fulfilled to the letter.

His report was startling to those of us who have been culturing the glands of scarlet-fever patients for some time. To determine the cause of scarlet-fever has been the aim of many workers and not a few of these included the glands in their investigations. Klein claimed many years ago that a streptococcus was the causal organism, and Gordon also leaned toward this belief. Class believes that the diplococcus described by him is the cause and later Mallory thought that his protozoon-like bodies found in the skin of scarlet-fever patients may be the cause. None of these claims, however, has been substantiated. The discovery of the exact cause of scarlet fever is certainly very much desired because then the paradoxes of this disease may be understood and its control and treatment made more effectual.

In a study of the glands of twenty-six patients with scarlet-fever, including a case cultured at autopsy, I did not find any organism, in any case, in any way resembling the bacillus described by Vipond.

After thorough sterilization of the skin overlying the enlarged glands a few drops of bloody serum were removed by means of an all-glass sterilized syringe. Cultures were made on coagulated blood-serum, plain and gelatin agar-agar and in bouillon. These were incubated at 37 C. and examined daily for four days.

The following twelve cases were cultured by the above method when the glands were enlarged sufficiently to be reasonably certain that one could strike and culture the gland by puncture. In only one of these, Case 3, was suppuration present. In this case softening had just begun and a streptococcus was secured in pure culture.

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*From the Laboratory of the Philadelphia Hospital for Contagious Diseases.

[1] Vipond, A. E.: Scarlet Fever, Preliminary Note of its Specific Microorganism, Arch. Pediat., 1911, xxviii, No. 7, 564.

Case 1.—Mary L., aged 3 years, admitted July 25, 1911, with scarlet fever of moderate severity, accompanied by general glandular enlargement. Two days later the cervical glands on left side were markedly enlarged and quite hard. Cultures gave growth of a diplococcus. No bacilli nor streptococci.

Case 2.—James C., aged 4 years, admitted July 22, 1911, with simple scarlet fever. Cultures of glands six days later were sterile.

Case 3.—Hyman H., aged 5 years, admitted July 24, 1911, with a rather severe attack of scarlet fever. There was well-marked enlargement of the servical glands, especially in the right side, with slight softening. Cultures of these glands yielded a growth of a streptococcus of the bacillary type.

Case 4.—Frank G., aged 5 years, admitted Aug. 3, 1911, on the fourth day of a mild attack of scarlet fever. Eight days later the cervical glands on the left side were enlarged to about the size of a pigeon's egg. Cultures sterile.

Case 5.—Martin W., aged 3½ years, admitted Sept. 5, 1911, with mild scarlet fever. Six days later a cervical gland on the right side was enlarged to the size of a marble. Cultures were sterile.

Case 6.—Hendel M., aged 3 years, admitted Sept. 3, 1911, with simple scarlet fever. Eight days later a gland on the left side of neck was enlarged to the size of a marble. Cultures were sterile.

Case 7.—Alice B., aged 4 years, admitted Sept. 1, 1911, with simple scarlet fever. Eleven days later the cervical glands were enlarged to a moderate degree. Cultures sterile.

Case 8.—Adolph S., aged 3 years, admitted Aug. 25, 1911, with scarlet fever of moderate severity accompanied by general glandular enlargement. Eighteen days later the cervical glands on the left side were enlarged to size of small marble. Cultures sterile.

Case 9.—Fannie S., aged 10 years, admitted Sept. 12, 1911, with scarlet fever of moderate severity, accompanied by general glandular enlargement. Cultures were made of cervical glands on same day which gave a pure culture of a streptococcus.

Case 10.—Molly K., aged 5 years, admitted Aug. 29, 1911, with simple scarlet fever. Eight days later the cervical glands on the left side were enlarged to the size of a pigeon's egg. Cultures sterile.

Case 11.—W. D., aged 3 years, admitted Sept. 13, 1911, with severe anginose scarlet fever accompanied by general glandular enlargement. The cervical glands on the left side were very much enlarged and quite hard. Blood-cultures gave pure growth of a streptococcus. Cultures of glands made two hours after admission yielded a growth of a streptococcus. Patient died in twelve hours. Glands were removed and cultures of these gave a growth of a streptococcus.

In none of these cases, cultured from the second to the eighteenth day of disease, were bacilli found. In three cases, or 27 per cent., streptococci were secured.

In the second group of fifteen cases cultures were made after the glands had been incised. It seems reasonable to suppose that these bacilli would be found even after the glands had softened and were discharging. The following organisms were secured, isolated and identified by ordinary morphologic and cultural characteristics:

Streptococcus alone in 3 cases.
Staphylococcus aureus alone in 6 cases.
B. pseudo-diphtheriticus alone in 2 cases.
B. pyocyaneus alone in 1 case.
Streptococcus and *Staphylococcus aureus* together in 2 cases.
Streptococcus and *B. pyocyaneus* together in 1 case.

Of the two cases yielding a pure culture of what we called "pseudo-diphtheria" bacilli, one had discharging glands for five weeks and the second for two and a half weeks. These bacilli were of medium length; solid; Gram-positive; non-motile; non-spore-forming; grew luxuriantly on agar-agar, yielding a heavy, white, moist growth; did not produce acid in Hiss serum-water mixture containing 1 per cent., respectively, of the following sugars: dextrin, saccharose, lactose, dextrose, galactose, glucose, levulose, mannite and inulin. Cultures were grown in 1 per cent. glucose + 0.5 bouillon for forty-eight and ninety-six hours and injected subcutaneously into 250-gram guinea-pigs. The pigs did not show any evidences of toxemia. These organisms resemble those found in about 70 per cent. of cases of suppurative otitis media complicating scarlet fever. These organisms do not resemble those described by Vipond.

THE INTESTINAL INFANTILISM OF HERTER*

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At the last meeting of the Association of American Physicians a year ago Dr. Christian A. Herter presented a paper on intestinal infantilism, a definite condition which he recognized, analyzed, and, after exhaustive study, published with a very complete description of its characteristics.

Notwithstanding the great amount of scientific work accomplished by Dr. Herter, it seems likely that his name will be perpetuated in connection with this condition of intestinal infantilism more than with any other work that he did, for he described a condition that was never before carefully studied, and thus established it as a distinct disease with characteristic symptoms, intestinal flora and changes in the urine.

The study of different types of dwarfs (see table) has only recently attracted much attention, and while different classifications have been made it is probable that the types described by different men under different names could really be brought together in a general and simpler classification had we fuller information concerning them.

TYPES OF DWARFS

SEXUAL: Small adults.
ASEXUAL (Infantilism):
    Infant type—Anangioplasia (Loraine).
    Adolescent type (Brissaud).
    Lymphatic.
    Mongolian.
    Thyroid—Cretinism.
    Achondroplasia.
    Intestinal (Herter).
    Hepatic (Cautley).
    Pancreatic (Bramwell).

All classifications agree that dwarfism should be divided into sexual, in which the sexual development is normal, and the asexual or infantile type, and under this latter head most of the cases are classified. Thus in France, Loraine has described a type of infantilism wherein the extremities are small, the head is large, and the individual has thus the infantile relationship in size between head, trunk and limbs, and this condition he believed to be due to congenital lack of development of the arteries. Brissaud, on the other hand, has described another type in which the head is small, the face long, the limbs long, indeed an adult type of body. A lymphatic type has also been described in France, in which the child grows very stout, and in which sudden death may occur from a violent shock.

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*Read at the annual meeting of the Association of American Physicians, Atlantic City, May, 1911.

The Mongolian type is familiar and evidently belongs in a category of its own. The cretin again is a distinct type of which we have full information.

Cautley mentions an hepatic infantilism occurring with cirrhosis of the liver, while Bramwell has reported one case of infantilism apparently due to lack of function of the pancreatic gland and cured by administration of the pancreatic extract, and this case of Bramwell's has clinically much in common with the cases classified by Herter; but as there is no record of any careful study of the urine and the bacteriology of the feces, it is impossible to say whether it would come under Herter's group. This individual, however, had large, fatty stools, the distended abdomen and the good appetite which usually are associated with the infantilism of Herter.

Herter published in 1908 a monograph on five children whom he had carefully studied, all of whom had certain intestinal symptoms, showing a change in the intestinal flora and a lack of growth. He stated that he had seen ten such cases.

HERTER'S CASES

CASE 1.—The first of his cases was a boy 8 years old, who did well until he was 3 years of age, when he weighed 31 pounds. Disturbed digestion with diarrhea then occurred, so that for the succeeding four years no gain in weight occurred, the weight varying between 25 and 28 pounds. There was moderate anemia, lassitude, good appetite, and large, soft, gray, gaseous stools.

CASE 2.—A girl of 9 years developed normally until the end of the second year, when certain gastric symptoms appeared, followed by impaired nutrition, retarded development and distended abdomen. There was moderate anemia with large, grayish, gaseous stools. This child weighed at 9 years 47 pounds.

CASE 3.—The third case, a girl of 4 years, when first under observation, was emaciated, abdomen distended and there was moderate anemia. The movements were large, acholic, two or three daily. Diarrhea was frequent when carbohydrates were advised.

CASE 4.—Boy of 3 years, did well for the first year, after which there was irregular intestinal trouble with diarrhea, anemia, distended abdomen, and large gray movements. Weight at 20 months was 16 pounds, length 31 inches.

CASE 5.—Girl 9½ years old, never did well; had measles at 18 months, after which she had digestive troubles with tendency to diarrhea, with soft, light-colored stools, abdomen distended, and carbohydrate incapacity. At 5½ years her weight was 21¾ pounds, height 35 inches. She was pale, her tongue was coated, and there was great listlessness. At 9½ years her weight was 33 pounds, height 38¼ inches, head circumference 20 inches.

The symptoms that Dr. Herter finds developed in these children are:

1. An arrested development of the body. The child stops growing as it stops gaining in weight. On the other hand, the mental development of the child is fair.

2. The marked abdominal distention is common in all of them, often with dilation of the abdominal veins over the upper part of the abdomen. There is usually a moderate anemia, and what is very characteristic, marked fatigue. The intestinal symptoms are a tendency to looseness of the bowels, with occasional attacks of diarrhea, often with fatty stools, although there may be but little fat in the food. They are apt to have an excessive appetite and thirst, an increased secretion of urine, and usually have cold hands and feet. Symptoms of rickets may be present.

3. The most interesting part of this study of Herter's is the result of the examination of the feces. Herter has found in these cases an absence of the ordinary bacterial flora of the intestines of young children; that the dominant organisms present are Gram-positive organisms; that the prevailing organism is the *Bacillus bifidus* of Tissier, an organism of the sort observed by Escherich in an epidemic of diarrhea in a hospital. With this Herter finds two others, the *Bacillus acidophilus* and the *Bacillus infantilis,* which latter may possibly be a variation from the *Bacillus bifidus.* The *Bacillus coli* and the *Bacillus lactis ærogenes* are infrequently found during the active stages of this disorder. The examination of the feces shows an excess of fat out of proportion to the amount taken in the food, a large amount of fatty acids and soaps.

4. The urine of these children also shows characteristic changes. The amount passed in twenty-four hours is large. There is a rise in the ethereal sulphates, a pronounced indicanuria and excessive phenol and the presence of large amounts of aromatic oxyacids.

Herter discusses the general indications for treatment of these patients. He finds gelatin particularly useful in increasing the weight.

Cases that undoubtedly come in this same class have been described by others, but without the careful laboratory investigations undertaken by Herter, which makes it impossible to classify them accurately. Thus, Huebner[1] publishes ten cases, some of which undoubtedly come under this classification, while Schultz[2] describes three cases.

Bramwell[3] described a case of what he called pancreatic infantilism. It was a boy of 18 years and 7 months, measuring in height 4 feet, 4½ inches, his weight being 67½ pounds, and having the appearance of a boy of 11, with a history of no growth since he was 10 years old. He was perfectly formed, bright, with a high-pitched voice, but with infantile sexual development. He gave a history of chronic diarrhea for nine years, with five or six large, liquid, yellowish-brown movements a day.

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[1] Huebner: Jahrb. f. Kinderh., 1909, lxx, Part 6, p. 68.

[2] Schultz: Jahrb. f. Kinderh., 1905, lxii, 794.

[3] Bramwell's Clinical Studies, 1903, ii, 348.

Dr. Bramwell demonstrated that the boy's pancreatic secretion was defective and that there was still a chance for growth, as the epiphyseal lines were unclosed.

Under treatment with pancreatic extract for two years the boy showed remarkable improvement, a gain in height of 5⅞ inches, a gain in weight of 23¾ pounds, with a normal sexual development. It was found on omitting the pancreatic extract that the diarrhea returned.

Bramwell was thus convinced that there is one form of infantilism due to disturbance of the pancreas that can be cured by the administration of pancreatic extract.

In a later contribution[4] he records a case of a girl of 20 who had the appearance of a girl of only 14 years. There was no pubic hair and no evidence of cretinism. She was found dead on a road, and autopsy disclosed that there was a chronic endocarditis, a uterus 1 inch in length; no ovaries were found; the kidneys were fused, forming a horseshoe kidney, and a pancreas that was large and extremely fibrous. No report of a microscopic examination of the pancreas is recorded.

Two cases were reported by Dr. John Thomson,[5] which were shown at Dr. Bramwell's clinic, and thought to be of the pancreatic type of infantilism. No later report of the result of treatment, however, has been found.

This one case of Bramwell's, then, which was similar to those described by Herter, so far as their symptoms are concerned, was apparently of definite origin and readily curable.

AUTHOR'S CASES

I have seen recently four examples of this condition.

Case 1.—The first case, a child now 4½ years old, has been under my care for twenty months. She had a history of never having done well. She had had repeated attacks of bowel trouble, from which she would convalesce only to be debilitated by a fresh attack. When first seen in August, 1909, she was suffering from intense general lassitude and would not willingly lift her head from the pillow. She would lie for hours without moving or speaking. Her mental development was very good but she evidently was lying thinking about her case all day, and after a physician's visit would repeat to the mother or nurse all that had been said about her case in her presence.

Her tongue was heavily coated, her abdomen was distended, she was markedly emaciated and somewhat anemic. She was having one or two very large, soft, gray, curdy movements, which would half fill the little chamber into which they were passed. Her appetite was very poor and she was put on a diet of peptonized milk with wheat flour gruel after an initial dose of castor oil. Bismuth was administered at each feeding.

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[4] Bramwell: Clinical Studies, 1907, vi, 175.

[5] Thomson, J.: Tr. Medico-Chir. Soc., Edinburgh, 1903, xxiii, 165.

The examinations of the feces and urine were made by Dr. Herter and corresponded to the findings in his cases.

She was under the care of a trained nurse for eight months and was taken to different places at intervals for a change of air. Her diet was gradually amplified and food such as meat, which she vomited when first tried, she was later able to take. During these twenty months she showed practically no gain in weight although at the time of the present report she weighed 2 pounds more than she did three months previously.

No food had been found that appeared to increase her weight although the gelatin advised by Dr. Herter was tried, but an improvement that must precede all others was evident in her case. The character of her stools improved, the greatest improvement having followed the administration of buttermilk, of which she took a pint a day. Her movements became of good color, slightly curdy, and but one of moderate size each day. She became interested in everything that took place about her. She constantly used her hands, stringing beads and other like occupations, and she would walk a little, although walking was still distasteful to her. Recent examination of the urine and feces by Dr. F. C. Wood still showed the characteristic condition described by Herter.

Urine: Sp. gr., 1,018; quantity 1,240 c.c.; no sugar; no albumin; trace of indol-acetic acid; very strong Millon's reaction; very strong indican; no Ehrlich's aldehyde reaction. It contained 200 mg. of creatinin and 29 mg. of creatin.

Feces: Feces contained indol but no skatol was found except on one occasion. The organisms present were almost entirely Gram-negative, with enormous numbers of *B. aerogenes capsulatus*, and no noticeable bifidus. There were present many of the large, oval, highly refractile bacteria referred to by Herter. Trypsin[6] not present but erepsin was found.

The administration of intestinal antiseptics had no influence on the bacteria of the intestines. Under the administration of pancreatic extract she seemed to improve more than under other medication.

Case 2.—A second case is that of a child of 2½ years that did well during the first ten months; at ten months it weighed 17½ pounds. In September, 1909, when 1 year old, after an attack of diarrhea, the weight fell to a little over 15 pounds. This child gained on two different occasions a pound or more, only to lose it again, so that at the time of the present report the weight remained about 15 pounds.

The child's stools, when doing badly, showed the characteristic gray color, and they always had a tendency to be loose. The child had an absolutely clean tongue, very little distention of the abdomen, and during a recent period her development had apparently been interfered with by the eruption of teeth, of which she cut seven in three months.

Examination of the feces and urine by Herter showed the characteristic condition, although there were some colon bacilli present in the feces.

This child did not gain on any modification of milk that was tried, and did not appear to do well on carbohydrates. Although she gained for a while on malt soup, she did best on a preparation of dried skimmed milk to which a moderate amount of fat was added in the form of cream. Afterwards when put on a mixed diet she gained for a short period. At 2½ years her weight was about the same as it was at 10 months.

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[6] In testing for trypsin in the feces the only reliable method seems to be that using coagulated sheep-serum either in a Mett tube or a Petri dish. When this method is employed, trypsin is usually found in the stools of children. In two of these cases of infantilism in which tests were made only small amounts of trypsin were found. Erepsin, however, seemed to be abundant in the watery extracts of the feces from both of these children. The simplest test for this ferment is the rapid and complete solution of casein, applied according to Gross' method. In all of these tests the proteolytic action of micro-organisms was excluded both by controls and by thoroughly saturating the solutions while in the incubator with toluol.

Case 3.—The child, 2 years and 5 months old, was a first living child after several miscarriages; birth weight 5 pounds, 2 ounces; did absolutely well with very little breast milk and accessory feedings of a cream whey mixture until 7 months old, when she weighed 15 pounds, 10 ounces. She then had an attack of vomiting, diarrhea and fever from which in a few days, however, she was better. She did not gain in weight and other similar attacks followed at intervals. A wet-nurse was obtained but still there was no increase in weight and there was practically none for many months although different sorts of food were used.

The examination of the feces by Dr. Herter showed the characteristic bifidus, which was very abundant in the fermentation tubes, as well as the *B. coli communis* and some cocci. The specimen of urine was unsatisfactory, as it had been mixed with the feces and was decomposed.

This then, was a case, like the second, which, while approaching this type, had not fully developed the characteristic condition a year prior to this report. Recently, without change in food or environment, the child began to gain in weight and developed normally, its progress being interrupted only by attacks of pyelitis.

Case 4.—The child was seen by me first when 3 years and 3 months old. She gave a history of attacks of colitis, had a distended abdomen, and although at that time of proper height for her age, the diagnosis of her condition was easily made from her history and the character of her movements. Careful examination of the urine and feces by Dr. F. C. Wood corroborated the diagnosis.

Her history was that of a child difficult to feed. When 5 weeks old she had not recovered her birth weight of 7 pounds, 14 ounces, and a wet-nurse was employed. She then gained fairly until she was 6 months old, after which, under the same wet-nurse, probably with insufficient breast milk, she remained nearly nine months with a gain of only 1½ pounds. The wet-nurse was then discharged, the child was put on a condensed milk mixture, and gained quite rapidly, weighing more than 28 pounds at 2 years, while at 2¾ years she weighed 35 pounds. She had had a diarrhea the previous summer from which she had recovered at this time. When 2¾ years old she developed clay-colored movements and became irritable. When nearly 3 years old the fatigue became marked, so that she objected to walking and she became less interested in what was going on about her.

Then another attack of colitis ensued, which, after a two weeks' interval, was followed by another one, and she was removed in August from the seaside to the mountains, where she seemed to improve. On her return I first saw her.

The child measured 36½ inches in length and weighed 24 pounds. She had a moderate color, was slightly anemic, her tongue was heavily coated, her abdomen was distended, this distention being largely due to dilatation of the stomach to within ½ inch of the umbilicus. Her movements were large, soft, curdy, yellow and offensive. She had some inflammation of the drum of her right ear which, however, quickly subsided under treatment. The stomach gradually contracted down, but the tongue remained coated.

She was put on a careful mixed diet, limiting the fats and carbohydrates.

The stool was strongly Gram-negative. The examination showed the *Bacillus bifidus*, a Gram-positive streptobacillus, the *Enterococcus proteiformis* and the colon bacillus, and also the *Bacillus aerogenes capsulatus*. No skatol was found in the stool, although there was a considerable quantity of indol. The sulphate partition showed a total of 0.76 gm. of preformed sulphates, and 0.035 gm. of ethereal sulphates, both in terms of SO_3. The ethereal sulphates were, therefore, about 1 to 20, which is within the normal limits.

The urine gave a strong indol-acetic reaction, showed a trace of indican, no reaction for aromatic oxyacids, and no Ehrlich aldehyde reaction.

Five months later the child came again under my care, having gone through the winter without any attacks of colitis, and it was then ascertained that for one year she had shown no growth. She had increased in weight at one time to 26 pounds but weighed now only 24½, and she was brought to me then because she was more fretful and because she complained of some pain in the buttocks and abdomen. She had in the interval been somewhat constipated but now was having frequent, soft, large, gray movements. Her tongue was somewhat coated and the stomach was dilated as when she came to me before. The large intestine was apparently not distended. She was thin and flabby but always had pink cheeks.

After castor oil, rhubarb and soda and a diminution of the amount of food taken, her stomach resumed its normal size in a week or ten days.

The urine, of which she passed 520 c.c. in 24 hours, was clear, pale, acid and had a specific gravity of 1,020. Millon's reagent gave no reaction of oxyacids; there was a faint trace of indol-acetic acid, there was no indoxyl and no Ehrlich's aldehyde reaction. A determination of creatin and creatinin was made and it showed an abnormal proportion between the two.

A later determination of urine and feces showed the following:

Urine: 670 c.c. in twenty-four hours, specific gravity 1,016, no sugar, trace of indol-acetic acid; very faint Millon's reaction; no Ehrlich's aldehyde. There was an excess of creatin.

Feces: The stool was dominantly Gram-positive and contained large numbers of the *Bacillus aerogenes capsulatus*, and some of the large oval, highly refractile bacteria referred to by Herter. There were also many Gram-negative organisms. Trypsin was present in fair quantity; also abundant erepsin. Indol, but no skatol was found.

The child was put on a pancreatic extract in fairly large doses, and showed improvement in the character of the stools and lessening of the abdominal pain, but did not show any material gain in weight.

The real nature of this disturbance is a matter of speculation. Dr. Herter expressed himself to me as feeling that it might be due to some lack of function in the pituitary body, and to determine whether this might be the case radiographs have recently been made in some cases, but with, so far as I know, negative results. To me it has seemed more likely that it was due to some damage to a part of the digestive system that has to do with the absorption of food. These patients have good appetites, take food and water eagerly, but have the large, poorly digested movements, with a great waste of fat.

In one case, at least, resembling these, that of Bramwell, the use of pancreatic extract seemed to be curative. But although this case was published in 1904, no reports of other cures from the use of pancreatic extract have been made. There were also two other cases of Dr. John Thomson's referred to as probably due to pancreatic disease and concerning these I find no published record of a cure.

These cases might be thought of simply as stunted growth, but it would seem to me, considering the previous history of diarrhea, the evidence of intestinal putrefaction, with the peculiar flora of the intestines, and the high ethereal sulphates in the urine, that the lack of growth is really due to an intestinal condition that interferes with a proper absorption of food in the bowels, and this interferes with an increase in weight.

It has been well shown by Fleischner[7] that in children under 2 years of age, failure to gain in weight is accompanied by a failure in proper growth. Thus Fleischner found that the average length of a baby weighing 9 pounds at 1 month is 22 inches, and at 7 months it is 23¼ inches, an increase of only 1¼ inches, while the normal gain for these seven months is some 5 inches in length, this being one-fourth of what it should be in a normal child. A 12-pound baby at 3 months measures a little more than 25 inches in length; at 12 months it measures only 26 inches instead of 29 inches, a gain here of only one-fourth of the normal increase in length. Thus the failure to absorb from the intestine would seem to explain both the failure to gain in weight and length.

CONCLUSIONS

The intestinal infantilism of Herter is not a very infrequent condition in young children, who for a considerable period will not grow or gain in weight, although the hygienic surroundings, feedings and supervision are most carefully managed.

These children have characteristic symptoms and characteristic, abnormal intestinal flora, as well as equally characteristic changes in the urine.

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[7] Fleischner: Arch. Pediat., October, 1906.

MYATONIA CONGENITA: A REPORT OF A CASE WITH AUTOPSY *

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Oppenheim[1] described in 1900 a remarkable disease in children the chief symptom in which is a hypotonia or even atonia of the muscles, combined with a corresponding diminution of the tendon reflexes. There is limitation of active movement varying in degree. In the most marked cases the extremities lie motionless and apparently paralyzed. On close observation contractions may be brought out in some or many of the muscles, but these are weak and without locomotor effect. In one of his cases the affection involved not only the muscles of the extremities, but those if the neck and trunk also. The condition is always more marked in the lower than in the upper extremities and the muscles supplied by the cranial nerves are not affected. Electrical stimulation shows a quantitative diminution of contractility up to its complete disappearance. There is no reaction of degeneration and no loss of sensibility. The joints are abnormally movable owing to the flaccidity of the muscles. It is a congenital affection, but it does not usually attract attention immediately after birth. He considers that it consists essentially in a retarded development of the muscles, and it tends to betterment or recovery. He did not, however, exclude the possibility of an involvement of the nerves or of the anterior horn cells. The muscles may be flaccid and soft, but they are never atrophied.

CASE.—*History.*—M. G., aged 6 months. The father was addicted to alcohol and was intoxicated at the time of conception and at intervals during the mother's pregnancy. During pregnancy the mother was well, but much worried and distracted over her husband's condition. There have been no miscarriages. The child of a previous pregnancy is healthy. The previous history of the mother is negative. The child, male, was born normally April 3, 1910. Fetal movements were felt during pregnancy and were quite as lively as those of the normal baby of the previous pregnancy. When the baby was three weeks old, the mother noticed that he seemed unusually limp, but was re-assured by the obstetric nurse in charge. When six weeks old, the mother noticed a dropping of one hand and that the hands seemed weak and limp and were not moved as freely as they ought to be. At this time she consulted a physician who said the condition was due to weakness, that the breast milk was probably not agreeing with the baby and advised that it be taken off the breast. When the baby was two months old he was seen by Dr. Howland of New York who noted a marked atrophy of the muscles of the trunk and extremities, and deformity of the chest. The baby seemed to improve somewhat, at one time being able to move his arms, but later this power disappeared. He has never been able to move his legs at the hips, knees or ankles, but could make slight movements of the toes and fingers. He has never been able to sit up or to hold up the head. The mental development is normal. The breathing has been labored since the baby was three weeks old and this has grown progressively worse. On September 3 the baby caught cold and since then the trouble in breathing became worse, with choking spells from mucus accumulation. To give relief the adenoids were removed on September 24. The breathing was somewhat improved by the operation, but has lately become as bad as before. The weakness increased until he could no longer nurse from the breast or bottle and has to be fed with a spoon. The baby gained weight up to the time of the adenoid operation, but since then has lost.

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*Read in the Section on Practice of Medicine of the American Medical Association at the Sixty-Second Annual Session, held at Los Angeles, June, 1911.

Physical Examination.—October 3. Poorly developed and poorly nourished baby. The cranium was square, the forehead prominent; the fontanels depressed but of normal size; the mouth, tongue and throat were normal. There were no teeth. The pupils were equal and reacted normally. The respiration was irregular, labored and wholly diaphragmatic, but not notably accelerated. The chest showed marked increase in anteroposterior diameter. The heart, lungs, and abdomen were normal. The baby was entirely unable to hold up his head and there seemed to be a complete flaccid paralysis of the trapezius muscle. The upper extremities were not moved at all from the shoulder and very feebly at the elbow and wrist. The hands hung over in flexion when the arm was held upright. There appeared to be a flaccid paralysis of the shoulder girdle muscles with marked atrophy, particularly of the pectoralis. There was slight atrophy of the muscles of the extremities. The knee-jerk was absent.

From this time until death, October 23, the condition gradually became worse, although there were temporary ameliorations. There was increase in the mucus accumulations and in the fits of choking, and the child died in one of these attacks.

Autopsy.—The body was that of a somewhat emaciated, male infant; the body length corresponding to age; the weight below the average; no rash on surface of the body; all the tissues were very soft and flabby to the touch; no rigor mortis; all the joints were extremely flaccid and movable. The bones of the extremities were easily felt through the soft tissues; no edema; the skin was normal. The subcutaneous fat was small in amount, soft and somewhat edematous. The muscles of the neck were thin but of normal color and consistency. The pectoral muscles and all the muscles of the back and extremities greatly atrophied. The atrophy did not affect the abdominal muscles to so great a degree. The pectoralis major was reduced to a small fascia-like band. The color of the atrophied muscles was grayish and translucent. They were more succulent and the single muscles were not easily dissected out. They seemed infiltrated with fat and fused with the surrounding connective tissue. The intercostal muscles were reduced to thin gray sheets. The abdominal muscles, though thin, had a better color than the others. The large muscle masses alongside the vertebræ were reduced to thin bands less than 1 cm. in diameter. There seemed no change in the nerves. They were of normal size and appearance and more prominent than is usual. The thorax was misshapen. The antero-posterior diameter was greatly diminished; the cartilages and ribs passed almost backwards from the sternum, then took an accentuation of the normal curvature, giving a flat depression in the antero-lateral situation. The lower border of the thorax flared outward like the mouth of a bell. The diaphragm was of normal color, thickness and consistency. It seemed rather better developed than normal.

The tongue, pharynx, larynx, and trachea were normal; the tonsils and lymphoid tissue of the tongue and pharynx of a development corresponding to age. All the lymph-nodes of the body were prominent. The thyroid gland was small but of normal appearance. The thymus was large, of normal color and consistency. It projected 8 cm. below the sternal notch and weighed 29.2 gm. The heart weighed 36 gm., and in all respects was normal. The aorta and other large vessels were normal with the exception of the left femoral, in which there was an occluding, fresh thrombus just below the origin of the profunda.

The entire upper lobe of the left lung and the upper posterior portion of the lower lobe were completely atelectatic and dark red in color. Nearly the entire upper lobe of the right lung was in same condition. There was no evident pneumonic consolidation, but all portions of the atelectatic lung sank in water. In the bronchi there was a small amount of muco-pus. The lower lobes of both lungs were normal; pleura normal; all the abdominal organs normal, as also were the brain and spinal cord on naked eye examination.

Diagnosis.—Anatomical diagnosis at autopsy, atrophy and degeneration of muscles, deformity of thorax, atelectasis of lungs, hypertrophy of thymus, fresh thrombus of femoral artery.

HISTOPATHOLOGY

The Muscles.—Portions of the various muscles were hardened in Zenker's fluid, liquor formaldehydi (formalin) and in Orth's fluid, sectioned in paraffin, and stained in methylene blue and eosin, in phosphotungstic hematoxylin and by the methods of Marchi and Weigert-Pal. All of the muscles affected showed the same changes though in a varying degree.

Cross section, hematoxylin and eosin: Section through some of the most altered muscles of the leg, with low power, shows the fibers arranged in well ordered fasciculi. The amount of connective tissue is increased. With low power, two well-defined masses of tissue can be seen. There are fibers which present the usual appearance of normal adult muscle. There are also masses of what seem to be accumulations of cells which are also arranged in fasciculi, but the masses are very much smaller than are the masses of normal muscles. Similar aggregations of cells are seen often at the periphery of a single muscle fasciculus. Occasionally, in the middle of the masses of small cells, single muscle fibers of the average size can be made out. At various places there are sections that appear to be the muscle spindles, that is, several muscle fibers enclosed in a definite capsule of connective tissue. The muscle fibers in the spindle vary greatly in size and the nuclei often show a central position.

Under the immersion, the larger fibers for the most part appear to be normal. Occasionally, the nuclei are found in the center of the fiber. What appeared under the low power as masses of small cells are seen to be composed of very small muscle fibers. Although most of these fine fibers are arranged in fasciculi, they are also found in the midst of the larger fibers and surrounding the groups of these. In the large fibers there is considerable variation in size, and they are usually round or oval. Many of the large fibers are vacuolated, containing either a single large vacuole, or several small ones. Some of these vacuoles contain a small amount of finely granular material. The largest fibers in this muscle are almost invariably definitely round. Occasionally, especially at the periphery of the muscular mass, fasciculi are found which seem to be midway between the larger muscle masses and the small fibers, but in general there is a sharp distinction between the two. With phosphotungstic hematoxylin there is a great variation in the muscle stain, some of the fibers being very much darker than others. The muscle fibrillæ are not well stained. In the fine fibers the fibrillæ are rather more prominent at the periphery of the fibers. On the longitudinal section of the muscles tissue, taken from about the same region, the same arrangement of the fibers can be distinguished. The cross and longitudinal striation is apparent in both sets of fibers, but more strongly marked in the larger fibers. The nuclei in the small muscle masses seem to be extremely numerous. They are of about the same size as in the larger fibers. Many of the fibrils are so small that when the section passes through a nucleus this occupies the whole extent of the fiber. The apparently great number of nuclei is due to the number of the fibers. When a single fiber is followed along, the nuclei are not more closely set than they are in the large fibers. The cross striations in a number of measurements are nearly the same distance apart in both the large and fine fibers. The length of the fine fibers could not be easily determined either by section or by teasing. They are never so definitely parallel to one another as in the large fibers. The masses of the large fibrils in longitudinal section are perfectly straight; the masses of the smaller fibrils present a wavy appearance as though they had not contracted at the same rate as the larger fibers. Most of the small fibers are solid and they do not present the appearance of embryonic fibers. Occasionally, however, fibers are seen which are hollow with fibrillæ at the periphery presenting much the appearance of embryonic fibers, and a fiber solid throughout most of its course may present an area where it has hollowed out. They also occasionally present swellings along their course, but as a general thing they preserve the same diameter.

Size of the fibers.—Measurements were made of groups of the larger fibrils, taking those of both the largest and smallest diameter. The average diameter obtained by taking the longest and shortest diameters in a group of fifteen adjoining fibers is 19.2 microns. The largest fiber found in the interior of the group is 35 microns. The average diameter of another group of fibers is somewhat more, 23.75 microns. In a small group of 22 fibers, there is a variation in the sizes of the fibers which belonged to the class of large fibers of from 8 to 20 microns. The average diameter of a group of twenty-seven of the small fibers, only one diameter being necessary on account of the prevalent round shape, is 3 microns with a variation of from 1.5 to 3.5. In the longitudinal sections, fibers are found from 1.5 to 4 microns in diameter. On comparing the cross striations, taking two adjoining fibers of the large and small group, there is a difference in the distance between Krause's lines, this being from 1.8 microns to 2 microns in the large fiber and 2.4 microns in the small, this being evidently due to a difference in the degree of contraction. This difference did not always hold, but a number of careful measurements showed in other places slight differences in the distance between the lines. Here and there among the small fibers in the longitudinal sections, single fibers are seen which show neither longitudinal nor cross striation. In these fibers there are here and there sarcous elements in the shape of double dots and occasionally rows of a half dozen or more of such dots separated by the usual interval between Krause's lines. Comparison of these fibers with the fibers of the diaphragm show that the average of the diameter of the diaphragm fibers is the same as the large fibers in the affected muscle. A study of the muscle by the Marchi method shows changes more marked in the large fibers. There is no general fatty degeneration. Single very small fat drops were commonly present, and in certain fibers there was a large amount of fat. The largest amount of fat was found in the otherwise unaltered muscle of the diaphragm. In the small fibers it was exceptional that any fat whatever was found. A study of the connective tissue in the muscle showed that this was relatively increased, but it is uncertain whether there is an actual increase in this tissue. There is no evidence at any point of any active cellular changes in the muscle. There are no phagocytic cells and no foci of lymphoid cell infiltration. The blood vessels in the muscle are normal, but of small size. The vascularity seemed small, relative to the amount of tissue.

An attempt at comparison of the size of the muscles here with those of children of the same age led to nothing of importance owing to the extreme variation in the size of the muscles in varying conditions of nutrition. Thus in a greatly emaciated child of six months, the average size from the measurement of 112 fibers of the Sartorius muscle was 5.1 microns. Measurement of the palatal muscles of a well nourishel infant at birth gave an average diameter of 17 microns; and the muscles of the larynx in a premature infant of seven months an average of 9 microns. We cannot definitely decide whether the size of the large fibers in this case varies from the normal, but probably it does not.

The nervous system.—Numerous sections made of the cortex, the cerebellum, the pons and medulla, and stained by the usual methods, showed in all respects a normal tissue. Sections of the cord at various levels, show very slight evidences of change. There seems no diminution in the number of cells in the anterior columns. The amount and distribution of the neuroglia is normal.

The Marchi stains show very slight degeneration of the myelin in the posterior columns. The degree, however, was so slight that in the routine examination of the cord it would probably have been unnoticed. The same applies to the anterior and posterior nerve roots, and to the spinal ganglia. In the Nissl stains of the cord, no certain evidence of cell degeneration can be made out. Sections were made of the sciatic nerve at various levels which were stained by the Marchi and Weigert methods and with hematoxylin and eosin. Here and there the sections stained by the Marchi and Weigert methods show very slight irregularity in the myelin. In single fibers there is a slight stain with the Marchi. There are no cellular changes in the nerve whatever. The examination of the nerves in the muscles show more marked changes. There are nerve bundles which are in all respects normal. The number of nerves, taking the whole mass of muscle, seems to be diminished, and among the fasciculi of small fibers, nerves are found which show evident degeneration and loss of myelin. A careful examination by the Weigert method leaves little doubt of the diminution of nerves in the changed muscle, that is, relative to the number of fibers. In these muscle fibers, no evidence is found of the terminal distribution of nerves to the single fibers. More or less definite nerve endings were found, however, among the fibers of normal size. Various branches of the sympathetic nerves which were found on the examination of the viscera, and branches of the pneumogastric nerves, were completely normal.

Sections of the atelectatic upper lobes of the lungs show congestion, atelectasis, edema, with small foci of bronchopneumonia. In the exudation here, a few diplococci conforming in morphology to pneumococci are found.

The myocardium is normal. An examination of the thrombus in the femoral artery shows this to have the usual composition of an acute thrombus, being made up of blood plates, fibrin, red corpuscles, and leukocytes. There was no examination of the blood made during life, but that within the vessels after death appears normal in the character and relative numbers of its cells.

The bone marrow of the femur shows a normal, active marrow.

It is very much regretted that there was no examination of the thymus. In the numerous pieces of tissue taken for examination, this was in some way lost. The numerous sections of the lymph-nodes show these to be normal with the exception of the almost complete absence of the germinal centers. The spleen is hyperemic, the follicles prominent, and in the germinal centers of these, almost without exception, there was extensive necrosis of a type exactly resembling that so commonly found in diphtheria. Microscopic examination of the liver, pancreas, adrenal, kidneys, intestinal canal and thyroid shows these organs to be normal. In the thyroid there is the usual amount of colloid.

ABSTRACTS OF CASES FROM THE LITERATURE

In view of the rarity and the interest of this disease, it seems worth while to give short abstracts of the cases hitherto reported.

Muggia.[2] Female child, family history negative. Pregnancy and birth normal. Directly after birth the child seemed normal. It cried, passed meconium, nursed and urinated. After a few days it was noticed that the child moved neither the arms nor legs. On observation, nutrition, size, weight and organs were normal. The limbs showed an absolute lax paralysis. The sensation of skin was normal. The superficial reflexes and the patellar reflexes were normal, but weakened. The electrical reaction of both nerves and muscles was not diminished. After four months' observation, there was no change in the condition and child continued to develop normally.

Batten.[3] These three cases reported by Batten, the first case following Oppenheim's articles, are properly considered by Collier and Wilson to belong to the group:

Case 1.—Male, age about 6 years; the third of four healthy children; never stood; could sit up but not kneel; was intelligent; on examination was thin and small; could get into sitting position; progressed by rolling over and over; no localized atrophy or hypertrophy; all movements could be performed with arms; unable to extend legs or to flex legs on abdomen; extensors and flexors of foot were fairly good; abdominal and dorsal muscles were weak. Contraction could be obtained in most muscles on strong stimulation, but not in quadriceps or gluteal.

CASE 2.—Male, age 7, small at birth, legs always contracted; never able to walk. On examination limbs were thin and wasted; long hands and feet; face somewhat expressionless, eyes prominent, facial muscles act; unable to walk; arms thin and wasted; muscles small; all movements could be performed; legs thin; knees could not be straightened owing to contraction of ham strings. Most movements could be performed, but legs could not be extended; knee-jerks absent; all muscles reacted to a moderately strong faradic current.

CASE 3.—Female, aged 6; could not stand or sit up, but could remain in sitting position; could always move both legs and could pick up small things with either hand; was intelligent. On examination, small for age, eyes prominent, sat up if placed, or lay on back with knees flexed; feet and hands appeared long; knee- and hip-joints could not be fully extended; muscular wasting general; muscular sense normal, knee-jerk and plantar reflex absent.

SCHULLER.[4] He demonstrated a child, male, age 19 months. The child was weak from birth. It learned to sit up and stand. After ten months, it was no longer able to stand nor to sit upright. On examination in addition to slight symptoms of rickets, there was a high degree of hypotonia of the muscles of the lower extremities, but without evidence of atrophy. There was absence of the deep reflexes; diminished electric excitability; active movements of legs could be carried out in but slight degree.

SPILLER.[5] Male, aged 22 months. The condition was first noted at five months; has never been able to hold anything in hand; at entrance into hospital child was well developed for 20 months old; muscles not wasted, but soft and flabby. The limbs were moved voluntarily at all joints, but the movements were very weak. There was a remarkable range of passive movements of legs, the feet could be placed behind the head while the front of thigh was in close contact with the trunk. There were no patellar or tendon reflexes; irritation by pin caused motion. The child had been constipated since 2 months old, which was attributed to weakness of the abdominal walls. The muscles reacted to the faradic current. Autopsy: No rigor mortis; muscles flabby. On cutting into calf muscles a great deal of subcutaneous fat and little pale muscle tissue were found; in sole of foot muscle almost absent. Microscopically the muscle fibers were small and those from the foot smaller than those from the back. The transverse striation was normal, the longitudinal not so well marked. The brain, spinal cord, and nerves were normal; no degeneration by Marchi stain. Spiller regards an arrest of development of the muscles the essential pathologic condition. Smith gives a subsequent report on the examination of the thymus.

OPPENHEIM.[6] Child (sex not stated), aged 1 year and 7 months; no hereditary trouble; soon after birth it was noticed that the child could not move its extremities though all the muscles supplied by the cranial nerves were normal. When 9 months old some movement of the arms was obtained, but the legs remained completely lame. The child was well developed and nourished. There was slight reduction in the volume of the muscles, which had a peculiar doughy feeling. There was diminution in the muscular tonus; the tendon reflexes in the legs were abolished, and the muscles did not respond to mechanical or electrical stimulation, with the exception of some feeble contractions in the peroneus.

BERTI.[7] CASE 1.—Boy, 3 days old. Two days after birth it was noticed that with the exception of the eyes, lips, tongue, and head, there was no motion. He lay with stretched limbs, crying weakly. The breathing was shallow and frequent, of diaphragmatic character. All the muscles of the extremities and the trunk with the exception of the diaphragm seemed to have no function. There was complete atony of the muscles. After three weeks the respiration was deeper. On stimulation there was slight motion of one arm. Subsequent history unknown.

CASE 2.—Girl, 5½ years old. On the day after birth it was noticed that the child, otherwise normal, seemed to show no life in the body with the exception of the head. After three weeks there was slight motion in one arm and in some of the fingers. After a year and a half the child could lift up the arms and there was slight movement in the legs. This condition lasted until 5½ years old, the child becoming emaciated. Now all movements are carried out slowly. She stands with legs spread out. The muscles are soft and relaxed. The electrical stimulation is diminished; knee-jerks sometimes doubtful; easily exhausted; no alteration in sensation, no sphincter trouble.

KUNDT.[8] Child, 18 months old. No hereditary trouble; two other children are normal; the pregnancy and birth were normal. The fetal movements were felt just as in the other pregnancies; mother noticed no movements of feet from the first; after six months there were movements of feet and lower limbs; thighs remained motionless; child could sit up, but could not stand. The arms were normal. The child was well nourished; subcutaneous fat abundant; the muscles were extremely lax on palpation. All passive movements of the hip joints easily carried out, but some opposition to extension of lower leg. The knee-jerk was absent. The Achilles reflex appeared on the left, but was imperfect on the right. Electrical stimulation produced contraction of the lower legs. After three months' observation a slight improvement was noticed. There was never reaction of degeneration.

ROSENBERG.[9] Male, 2½ years old. Family history negative. Mother did not feel fetal movements during pregnancy. Pregnancy and birth normal. Child nourished by bottle. The arms, head, face, and eyes moved normally. The child sat up at seven months. At eleven months on attempting to stand there was no strength in knees or hips. Child at time of report could not stand or walk. In other respects it was normal. The upper and lower legs could not be moved. The feet and toes could be actively moved. When a leg was lifted it fell as a dead weight. Contractions in the apparently paralyzed muscles were produced by pain. The legs showed no atrophy. There was entire absence of muscle tone and very extended passive motion could be made. The feet could be brought in contact with the ears. Palpation showed a decided difference between the affected and the normal muscles, the former having a soft doughy feeling. There was absence of knee and Achilles reflexes. There was complete absence of electrical reactions in the gluteal, in the quadriceps and in the adductors. In the lower leg only the peroneous gave a reaction. After six weeks' faradic treatment some improvement was noted.

IOVANE.[10] Male, aged 3 months. Family history negative, normal pregnancy and delivery. Child appeared healthy and took the breast. On the first day it was noticed that there was no voluntary movement of the arms or legs and that the head rolled about on the trunk. When seen at three months, there was flaccid paralysis with absolute atony of muscles of arms and legs; feeble movement at wrist; muscles of trunk atonic, only abdominal reflexes present; slight response to faradic current, none to galvanic. Child died at five months with bronchopneumonia.

SORGENTA.[11] Both children by the same mother. No movements during pregnancy. In both clinical history about the same. Both well developed at birth and from birth unable to move arms or legs; absence of cutaneous and deep reflexes; no reaction in muscles of legs; weak in arms. Death in one on fortieth day, in other on fifteenth day. In both cases convulsions preceded death. No autopsy.

These cases of Sorgenta have been excluded by Collier and Wilson, chiefly in view of its familial type and classed with the myopathies.

COMBY.[12] Male, aged 8 years. When seen first in September, 1905, could neither walk nor stand; kyphosis on sitting; intelligence good. The only defect was in the muscles, which were soft, but not atrophic; could move legs but they were not strong enough to support him.

CATTANEO.[13] Female, aged 4 months. Birth normal. Fetal movements not felt. Breast fed. After birth it was noticed that the child could not move hands or arms. Father thought it could move arms at time of report. Could not hold head up. Observation showed a well nourished child; only slight movements of hands and feet; cutaneous and deep reflexes absent; electrical reactions diminished.

BING.[14] Male, 3½ years old. A typical case. It was at once noted that the legs were passive appendages to the body and could be moved readily in all directions. A normal birth. Congenital bilateral pes varus. Great weakness of muscles since birth. Child could neither stand nor walk. Arms could be moved, but movements weak. Head could be held but a short time in one position. Knee-jerks absent, no disturbance of sensation or of sphincters. Bing removed a piece of muscle but does not state from which part and found it normal, although there might have been some question whether the nuclei were not more abundant than normal. He questions whether the condition is to be regarded as functional or due to a non-development of the spinal cerebellar tract which governs the tonus.

TOBLER.[15] Male child, the first born. First observed at 20 months and under observation three years. Fed on breast for six months. From the first the loss of motion was striking. Examination at 20 months showed a well nourished child. All extremities in condition of complete atony but no paralysis; some motion in arms but slow and weak. Atony even extended to facial muscles, but the movements of tongue and eyes were normal; electrical stimulation greatly diminished and in part lost; sensation not affected; intelligence good; no change during continued observation for three years. Death probably from diphtheria at 5 years. No observation as to fetal movements.

VARIA AND DEVILLERS.[16] First child; fifty-nine days before birth mother fell and was laid up with periostitis until eight days before birth. During pregnancy, both before and after the accident, fetal movements were felt; child under observation for nine months; female child; arms and legs immobile; all the muscles abnormally flaccid. The head rolled about indifferently when not supported. There was spinal kyphosis when child was seated, which disappeared on lying down. Death from bronchopneumonia when 9 months old. (Pieces of muscle and cord were sent to Dejerine for examination but no report has been published.)

COMBY.[17] Male, aged 4 months. When one month old the child had an attack of diarrhea and it was then noticed that the muscles were paralyzed. When examined, legs immovable; no muscular wasting; knee-jerks absent; no support for head; electrical reaction showed hypo-excitability of right leg; no reaction of degeneration. After a year muscular atony persisted.

CARY COOMBS.[18] Female, aged 10. Flabbiness of one hand noticed one-half hour after birth. Nothing further was noticed until time to walk. Then it was found that the legs would not support her; could not walk by herself until 2 years old; arms most affected; ankles often turned causing her to fall; extraordinary flaccidity of all joints; knuckles could be made to touch the back of the wrist; lower limbs very hypotonic, but not so much so as upper; knee-jerks and tendon reflexes were present; electrical excitability was diminished. Muscles could be distinctly felt, but they were small, soft and doughy.

LECLERC.[19] Female, aged 4 years. Mother felt fetal movements as in the case of her other children. For the first days the child appeared normal. A bronchopneumonia developed at 6 weeks of age and after this the paralysis was observed. The child then appeared completely paralyzed, incapable of making any movements of extremities. Head falls on shoulders when moved. From this time a slow but progressive improvement took place. At the time of the report the child could move the limbs, but the movements were feeble. Not a true paralysis, but muscular atony. The face and all muscles innervated by cranial nerves were normal. The passive movements of the joints were greatly exaggerated. The muscles were not atrophied, but seemed extremely soft. The intelligence was slow in developing.

BAUDOUIN.[20] Child, 4 months old, female. Pregnancy and birth normal. Since birth neck, trunk, arms, and legs were immobile. Muscles supplied by cranial nerves normal, except for slight internal strabismus of right eye; complete flaccid paralysis in trunk and limbs with the exception of feeble movements of fingers and toes; absence of deep reflexes; respiratory muscles were affected. The thorax dilated very slightly during respiration. Faradic excitability was diminished. Death from bronchopneumonia. (Baudouin says that the disease tends naturally toward recovery and if cases are met with early a complete recovery is possible, which is somewhat at variance with the results of his autopsy.) He found in the cord at the level of the eighth cervical segment that the cells of the anterior horns were diminished in volume but there was no evidence of neuron phagocytosis. He thinks there is probably an arrest of development. Section of the anterior and posterior nerve roots showed the anterior four or five times smaller than the posterior. The posterior stained more deeply than the anterior. In the anterior root the sheaths were more widely spaced and separated by amorphous tissue. Sections of the sciatic nerve stained with Marchi showed no fragmentation of the myelin. In sections stained by Weigert's the nerve was not well stained, the myelin sheaths were thickened and not equal in number in the different bundles. He concluded that with the myelinated fibers there were numbers of nerves not yet myelinated. The same lesions were found in the crural, cervical and median nerves. The condition in the nerves was not a neuritis but an arrest of development and a retardation of myelin formation.

The muscles presented very profound lesions, varying little according to the muscle examined. The connective tissue sheaths were numerous and thickened. The vessels were normal, but often surrounded by young cells. The muscular fibers were much changed. There were masses of small fibers from 6 to 8 microns in diameter and along with these very large fibers often reaching a hundred microns. The nuclei were increased in number and often lay in the interior of the fibers. The striations were normal and there was no degeneration. The diaphragm was the least affected. The skin was normal, the lungs showed disseminated bronchopneumonia. There was slight sclerosis of spleen with follicles more accentuated than normal. The thyroid gland was sclerosed and contained no colloid. There was sclerosis of the thymus with small Hassall's corpuscles. The condition was due to some cause which had suspended the development of the marrow and the nerves, and through these changes the muscle had become affected.

AUSSET.[21] Female child, 2 years, 9 months old. Mother had five children, two born dead. No fetal movements during pregnancy. After birth the mother noticed that the child was unlike others. It was inert and lay five or six hours without demanding the breast; did not move limbs even when crying; there was slight movement of arms. At 18 months there was some febrile disturbance and at two years whooping-cough. On observation, nutrition appeared good; fat abundant on lower legs; slight movement of arms; legs immovable; no actual paralysis; when leg was lifted it did not drop as rapidly as would a paralyzed leg. The joints were not abnormally movable. The left leg was smaller than the right. The electrical reactions were normal.

BRUNARD.[22] Child aged 2 years. External appearance was that of a well nourished infant rather deficient in fat. No hereditary trouble. Birth normal; fetal movements felt; breast nutrition. At the age of 2 months there were convulsions which had not reappeared. The first teeth were late in appearance. The attitude was striking. The child lay on her back, the legs flexed on the thighs, with total abduction. The extremities could be moved, but the child could not take hold of an object; could not walk; gave picture of child sitting down, the body bent forward, the face on the ground between the feet. The patellar reflex was absent; electrical reactions did not appear to be diminished; no trouble with respiration, circulation or digestion. The child was idiotic. (In this last the case departs from the type, since all the other cases showed normal intelligence.)

Collier and Wilson.[23] Case 1.—Boy aged 4. Normal pregnancy and birth. No mention of fetal movements. At birth well-shaped but thin; breast fed. The position assumed naturally from birth was one of flexure of hip and knee and extreme dorsiflexion of ankle; legs and arms weak and limp; could not hold head erect. On examination, a small, thin, soft, limp child; muscles small and absolutely atonic, the joints so relaxed that the limbs could be placed into all sorts of fantastic positions without discomfort. The muscles have a soft, velvety feel. A limb held up by its proximal end can be shaken like a flail. There was contraction of the iliopsoas, adductors, and ham strings on both sides. With this restriction, all voluntary movements could be performed quickly and with normal range, but the power was very feeble. The vertebral column bowed in the sitting posture but the curve disappeared when the child was held by the shoulders. The soles of the feet were almost flat, soft and like long pads. Faradic and galvanic excitability was lowered. The deep reflexion without exception were absent.

Case 2.—Boy, aged 7. The mother was weak in the limbs when a child, and several members of her family could not close the eyes properly. Birth normal. No mention of fetal movements. Soon after birth it was noticed that the child was unnaturally limp and could not hold up his head; had never been able to walk; slow improvement since three years old. On examination, head large, facial muscles weak, inability to close eyes properly; universal flaccidity and weakness; the muscles were soft and weak; impossible to differentiate muscle from adjoining tissue by palpation. All muscles contracted voluntarily, but too feebly to do any useful act. All reacted to faradic current. Child had a peculiar triangular face and open mouth which may have been due to maldevelopment or to muscular contraction preventing the full growth of the mandible. The superficial reflexes were normal, the deep entirely absent. There had been gradual improvement and when last examined the child could walk a little without support.

Case 3.—Boy, aged 5½ years. Family history negative. Child breast fed. Nothing noticed for six months with the exception that the child placed his limbs in extraordinary positions. After this the mother noticed that the legs were weak. He finally was able to stand when holding on to something; then became weaker and weaker in the legs. On examination, a pale, thin child, of average height; intelligence good; no difficulty in speaking and swallowing. Muscles of upper extremities were small but all voluntary movements could be performed. There was absolute hypotonia of all the muscles, with relaxation of the ligaments and flail-like joints. Muscles of the neck and trunk were thin and weak. He could raise his head only when lying in the supine position and sat up with difficulty. In the lower extremities there was slight contraction of the flexors of the thighs and decided contracture of the muscles of the feet. The faradic excitability of the muscles was diminished. The superficial reflexes were normal; the deep, entirely absent. Continued improvement occurred.

Case 4.—Girl, aged 1 year, 8 months. Family history negative; pregnancy and birth normal; fetal movements felt; breast fed; child normal until 12 months old. At this time she was ill for a month with an attack of bronchitis. At end of illness it was noticed that she could not move her legs; arms not affected. On examination, a thin but otherwise fairly developed child; motion of upper extremities normal, but weak and flaccid; the muscles of the lower extremities were absolutely atonic; movements very weak; considerable voluntary control; a flail-like condition of the joints; the deep reflexes were absent; the faradic excitability was diminished. After being at the hospital for three months marked improvement in the power of all muscles was noticeable. (The cases of Collier and Wilson are rather different from the other cases which have been reported, in the age of the patients, in the slighter degree of the muscular involvement, and the time after birth of the development of the condition.)

Gastonguay.[24] Child aged 3 years and 8 months. Mother perceived no fetal movements; nothing abnormal noticed for six weeks; then after a pulmonary attack the child appeared completely paralyzed with the exception of the face and pharynx. Child nursed and drank perfectly. When seen there was no complete paralysis, but atony of the muscles. This atony extended to the ligaments, rendering the joints much more flaccid and giving greatly exaggerated passive motion. The muscles did not seem atrophied but were much softer than normal. All muscles enervated by the cranial nerves were intact. The skin was not very supple, that of the lower extremities showed a hard, smooth edema. The mental development was retarded. Slight improvement occurred while under observation.

Lereboullet and Baudouin.[25] Child, aged 11 months. Flaccid paralysis having its maximum in the muscles of the neck. Head rolled unsupported. The extremities were equally affected; reflexes diminished but not abolished. Death, with fever and dyspnea, due to a beginning pulmonary septicemia. Convulsions were seen and during these the flaccidity gave place to contraction. Autopsy: The cord and brain were examined by methods of Nissl and Marchi. These were found normal. No diminution in size or number of the cells in the anterior horns. The muscle lesions were marked, particularly in the neck muscles. The fibers were of irregular size. The transverse striations were absent; the longitudinal present; a considerable increase in nuclei.

Laffer.[26] Girl, aged 8 years. Birth normal. Soon after birth, it was noticed that the face was immobile; could hold head erect when a few months old, and sit up when 7 months; began to walk when 14 months old, but with a peculiar waddling gait. There had been slight improvement since. There was great flaccidity of joints, particularly those of the lower extremities, and muscular weakness. (This case offers differences from the other cases in the first appearance of the condition in the face. There was no note of flaccid atony in the lower extremities until she began to walk at the age of 14 months.)

Rothmann.[27] The first child of the mother. The mother fell on her back in the eighth month of pregnancy. Fetal movements were felt but were weak. When 14 days old the mother observed that it did not move the limbs, and thought the condition was present from birth. The child when seen at 4 months was a typical case. A badly nourished child of normal size. Skull, otherwise normal, showed closure of the large fontanel. The legs were relaxed and showed no trace of active motion. On the upper and lower legs the skin was thick, the fat abundant; the muscles could not be palpated. The legs could be moved in any direction without opposition. The skin and tendon reflexes of the legs were absent. The arms could not be actively moved. There was movement of the fingers. The head fell to one side or forward or back on the body when moved. The face, the pharynx, the tongue, the eyes, all moved normally. There was no paralysis of the sphincters. Electric stimulation procured effect only on flexors of arms. When crying the expression was normal.

Autopsy. The thymus was large for the age of 5 months. The cord was small and firm. Microscopically the cord showed extensive disappearance of the large motor ganglion cells of the anterior columns. The few motor cells which were retained were smaller than normal and showed evidences of degeneration. The absence of all fresh degeneration showed that the condition must have lasted several months. There was also a diminution of cells in Clark's columns. The white matter was entirely normal. In the vicinity of the hypoglossal nucleus there was chromatolysis and apparent beginning of the process. The investigation of the peripheral nerves of the arm and leg showed diminution in the size of the fibers, with thickening of the perineural connective tissue septa. There was no degeneration. The nerve fibers in the muscle were made out by the gold chlorid method; the end plates were not seen. Since according to the condition of the anterior horn cells only few motor fibers could be present, they must either have vanished without leaving a trace, or there must have been a regeneration in fetal life. The biceps showed increase of the connective tissue with increase of nuclei. In the quadriceps there was infiltration of fat between the fibers with small-cell infiltration. The intercostal muscles were normal. The thymus showed an increase in the Hassall bodies and thickening of the walls of the vessels.

COLLIER AND HOLMES.[28] Child, aged 3½ years. Pregnancy and birth normal. No mention of fetal movements. Mother noticed that the child did not kick like other children, but no other peculiarity was noted until a year old, when she tried to stand him up and found that his legs doubled up under him; was never able to stand or to walk; could not himself assume a sitting position. The diaphragm and intercostals acted well. There was no local muscular wasting. Passive movements at all the joints was free, and flail-like movements of hands and fingers could be produced by shaking. In the lower extremities hypotonicity of muscles of thigh and calf. The feet could be easily touched together behind the head. Deep reflexes absent; superficial, normal. From this patient a piece of thigh muscle was taken for examination, as well as from one of the previous patients of Dr. Collier, who had died from bronchopneumonia. No mention is made of the examination of other tissues and there is no general account of the autopsy. The muscles were fixed in Zenker's and sections made. The muscles appeared very pale and infiltrated with fat. Very few spindles could be found in the more severely affected muscles. The majority of fibers were much reduced in size, and showed an average diameter not exceeding twelve microns on cross section; they were irregular in shape, the cross striation well preserved. The nuclei seemed to be largely in excess of the normal. A small number of fibers were enormously enlarged, up to 150 microns. Regressive changes were present in many of the hypertrophied fibers. There was great increase of connective tissue in the affected muscles. The muscle bundles were normal. The intermuscular nerve fibers were small. The muscle changes are the essential pathologic lesions. They may be regarded either as due to regressive changes in previously normal fibers, or as due to defective development. He gives photographs of the slides which show an almost identical condition with that seen by us, with the exception of the size of the fibers, that of the atrophic fibers being 12 microns. The autopsy description was limited to the muscles.

J. P. CROZER GRIFFITH.[29] At a meeting of the Philadelphia Pediatric Society Griffith showed a typical case in a boy about 17 months.

ASHBY.[30] Girl aged 8 years. Condition existing from birth. The patient lay in bed as if completely paralyzed. All muscles of the body, including face, were flabby and wasted; difficulty in masticating solid food; reflexes feeble; electrical reactions normal; all special senses normal. The condition gradually improved. (This case departs from the usual type in the involvement of the facial muscles and those of mastication.)[33]

SYMPTOMATOLOGY

The description of the disease first given by Oppenheim covers very well the main points in the symptomatology. All reports agree as to the flaccid paralysis, most marked in the lower extremities, and the general non-involvement of the muscles supplied by the cranial nerves. The only possible exceptions are a difficulty in deglutition in two cases, and in one an inability to close the eyes. The great flaccidity of the joints, which might be supposed from the condition of the muscles, is also generally described. No description of this can be better than that given by the mother of one of Collier's patients: "By whatever part of the body I held him up, all the rest of him hung down like so many pieces of yarn." When we consider the remaining symptomatology there is much uncertainty. Sensation in the affected parts seems on the whole to be unimpaired, but an abnormal tolerance of strong faradic currents has been mentioned. The reflexes may or may not be present. Contractility is generally produced by the faradic current, and there is absence of the reaction of degeneration.

ETIOLOGY

There is no accurate knowledge of the onset of the disease, whether sudden or gradual. In all the descriptions it has been impossible to give any exact time so that the onset must have been gradual; possibly weakness preceding atony, and a gradual extension of the field; in some of the descriptions this is evident. Oppenheim and those following have laid weight on the congenital nature of the disease as being one of the important conditions belonging to it. Certainly this is involved in much doubt. It is true we know nothing of the time a muscle degeneration may be in progress before symptoms are produced, but if we assume that the beginning of the disease is coincident with the appearance of the flaccid paralysis, then it certainly is not usually congenital. Of all the cases, in but five it is stated that it was present at birth. An important point bearing on its congenital nature is that of the fetal movements of the child. The degree to which this is felt varies and its absence does not denote fetal paralysis. In the cases we have collected, the presence or absence of fetal movements is mentioned in ten. In these the fetal movements were felt in seven and were absent in three. The usual statements of the time after birth are vague. The time extends in one case to seven months, in another ten, in another twelve, and in one case seven years. In regard to the frequent cases in which the condition was noted from two to thirty days after birth, it does not seem probable that it could have been present from birth and escape the attention of the mother, the nurse and the physician. We have asked several obstetricians with regard to this and they have not thought it possible. The mothers who have been asked have with some heat denied the possibility, and have even regarded the question as an attempt to secure antisuffrage evidence by showing in the female gross deficiency in the powers of observation. In none of the cases has it appeared in connection with an acute infection. In four cases it is stated that it appeared after a bronchopneumonia, and after diarrhea in one. In view of the frequency of these conditions, there is evidently no relation. It is scarcely possible by symptomatology alone to make a disease entity. To that belongs first a proved etiologic factor, or in the absence of this, definite pathologic lesions.

PATHOLOGY

There have been six autopsies made on cases and in two additional cases examination of the muscles, and there is much disagreement as to the character of the lesions. In one of the autopsies by Baudouin there was diminution in number and degeneration of the anterior horn cells and absence of myelination in the nerves; in another, the case of Lereboulet and Baudouin, the cord and nerves were normal. In Rothmann's case there was marked involvement of the anterior horns and the nerves. In Spiller's case, in ours, and in one of Baudouin's, the cord was normal. Presumably it was also normal in Holmes' case, since he makes no mention of its examination.

There is much more unanimity in regard to the condition in the muscles. Spiller regarded this as due to imperfect development, and most descriptions mention the great diminution in size of certain fibers and the great enlargement of others. Holmes found fibers up to 150 microns in diameter, and Baudouin found fibers of 100 microns. The photograph which Holmes gives of a cross section of muscle certainly shows no such fibers and might have been made from a section of the muscle in our case. Bing found the muscle normal, though there might have been some question of a nuclear increase. Such variation in the anatomic lesions are akin to the variations in the symptomatology and are not sufficient to serve as a basis for the creation of a disease entity. Even in the case of the lesions in the muscles, there are a number of conditions which produce similar lesions, as the great atrophy of certain fibers with a normal condition, or an enlargement of others.

The condition of the thymus gland is interesting. It was found to be enlarged in Spiller's, Baudouin's, Rothmann's and our case. Whether there is any relation between the thymus and the condition is uncertain. We regret that no microscopic examination of the gland was made in our case. Spiller and Smith[31] found fibrosis, enlargement of the Hassall bodies, endothelial proliferation, and arteriosclerosis. Baudouin found sclerosis with diminution in the Hassall bodies, and Rothman enlargement of the bodies with thickening of the walls of the blood-vessels. To any one who has made many examinations of the thymus, these statements do not convey anything. There is no organ in the body which varies so enormously in size as does the thymus in children under one year. We have taken from the records of the pathologic laboratory, Harvard Medical School, the weight of the thymus in sixty autopsies on children under 1 year of age and found a variation from 1 to 26.5 gm. The average is 4.5 gm. There is no record of weight equal to that of the thymus in this case, the next highest being 26.5 gm. in a child of four months with status lymphaticus.

There is no reason to believe that the disease is an infectious one. The onset, the distribution of the lesions, and the absence in our case of any changes which might show a past infection even, all speak against this. The lesions are not focal. Neither single muscles nor single muscle groups are affected. All the muscles innervated by the spinal nerves are affected though in different degree. The disease has further never been seen in an epidemic or in an endemic form. The reported cases are generally distributed and have become more numerous in late years because attention has been more attracted to the disease.

It seems much more evident that the disease is toxic rather than infectious and that in certain cases, at least, the action of the toxic agent is either directly on the muscle fibers or on the terminal nerves or nerve endings. It also seems probable that such a toxin is produced not in the infant but in the mother. There does not seem to be any relation between the disease and any other disturbance in the child, no relation to food or digestive disturbances. Some of the children were fed on the breast, others on the bottle; generally the children were healthy at birth. It is perfectly possible to conceive of the presence of a toxin in the blood of the mother from the action of which she would be protected by the presence of antibodies. The toxic agent would be transmitted along with the protecting antibodies through the placental circulation. After the birth of the child the action of the toxin would not be counteracted by the antibodies which are no longer received from the mother. We can conceive of such a toxin acting either on the spinal cells or on the nerves or on the muscles, or on all three tissues, of its being constantly present in the mother's blood, which would be the case in the Werding-Hoffman[32] familial type, or only temporarily present as in the cases of myatonia. It is, of course, difficult to explain under such an hypothesis why single muscle fasciculi and single fibers in a fasciculus should remain normal as in our case.

PROGNOSIS

The prognosis in these cases is doubtful. Without actual destruction of nerve cells there should be considerable capacity for regeneration, and improvement has been seen in many of the cases. We do not know, however, whether muscles so altered as these are capable of complete regeneration. The few reports of cases up to 10 years of age do not seem to give a very good prognosis. Of course much will depend on the extent of the lesions.

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PROGRESS IN PEDIATRICS

DISEASES OF THE CIRCULATORY SYSTEM

Congenital Heart Disease

A Review of Recent Literature

From a clinical study of fourteen cases of congenital heart disease Walker[1] draws the following conclusions: (1) By a careful examination of the physical signs in patients suffering from congenital morbus cordis, it is probable that, with the accumulation of details, such cases will be divided into clinical groups of distinctive types, and that eventually when such clinical groups have been established and the morbid conditions associated with them described, the diagnosis of one lesion from the other, and the prognosis based on it, will be possible. (2) Exclusive of other lesions, such as septal defects, there appear to be at least three clinical groups of pulmonary stenosis: I, *a*. Cases in which the signs seem to indicate a constriction in the neighborhood of the pulmonary valve; high stenosis. I, *b*. Cases in which the signs seem to indicate a constriction and incomplete fusion of the infundibulum with the body of the right ventricle; low stenosis. II. Cases in which there are evidences that the ductus arteriosus is also patent. (3) Patent ductus arteriosus may give rise to a water-hammer pulse and capillary pulsation. (4) In many cases of congenital heart disease, and more especially when there is evidence of ductus arteriosus patency, an abnormal zone of basal cardiac dulness is present. (5) There seems to be evidence that where pulmonary stenosis is accompanied by patency of the ductus arteriosus the symptomatology is less severe and life more prolonged. (6) A large percentage of cases of congenital heart disease, associated with pulmonary stenosis, give a definite history or family history of rheumatic infection, or a history of cardiac disease in other members of the family.

Goodman[2] reports a case of patent ductus arteriosus in a boy aged 14, of good mental development, apparently healthy, exhibiting no subjective symptoms of cardiac disease and showing no cyanosis or clubbing of the fingers. He considers the following points, in this case, of diagnostic importance, but cautions that too much weight should not be placed on any one sign or symptom: Of the physical signs, emphasis is laid on the bulging of the left side of the chest, visible pulsation in the second left interspace and a systolic thrill in the same area not felt elsewhere. Here is to be heard a loud, rasping, grating systolic murmur, appreciated a short distance from the heart, transmitted to the carotids, better to left than to right, and heard well in the interscapular space at the level of the spine of the scapula, and along the vertebral column; hypertrophy of the right and left ventricles with a "band-like area of dulness" along the left margin of the sternum between the second and fourth ribs; pulsus paradoxus; normal pulse tracing; paralysis of left vocal cord; Röntgen-ray confirmation of Gerhardt's dulness. Goodman has collected from the literature seventy-one cases, practically all the cases reported from 1847 to the present time, and has analyzed them from the point of view of symptoms and physical signs.

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Z. v. Bokay[3] reports a case of transposition of the large vessels of the heart in a child 9 months old. The aorta arose from the right ventricle and the pulmonary artery from the left ventricle, making two circulatory systems whose only connection was a patent foramen ovale. The wall of the left ventricle measured 4.5 mm., the wall of the right ventricle 10 mm. Clinically there was marked cyanosis and a systolic murmur at the apex. The author has collected from the literature forty-three similar cases and tabulated them according to age, clinical symptoms and autopsy findings.

Kingsley[4] reports the case of a female infant 5 months old in which, together with other congenital deformities, a patent ductus arteriosus was found.

Weber and Dorner's[5] case of congenital pulmonary stenosis in a young man aged 29, is of especial interest because of the blood conditions. There was marked cyanosis, an absolute polycythemia and a true plethora (polyemia); that is, the amount of hemoglobin and the number of red cells per cu. mm. of blood and the amount of hemoglobin and volume of blood per 100 gm. body-weight were greatly above the normal. They believe this increase is due to increased formation in the bone-marrow. The blood-plasma was only very slightly concentrated. Orthostatic albuminuria was marked in this case, a condition not found in most cases of congenital heart disease. Bie and Maar[6] have recently reported a similar case.

Warthin[7] believes that congenital syphilis of the heart is not a rare disease. The disease rarely manifests itself in the form of a gumma, but most frequently in the form of a diffuse interstitial myocarditis due to the presence of the *Spirochæta pallida* in large numbers. The diagnostic criterion is the demonstration of spirochetes in the fibroblastic areas in the heart wall. There is no characteristic macroscopic change, so that the absence or presence of congenital cardiac syphilis can be told only by a thorough microscopic examination. A series of twelve cases is reported, nine of which occurred in infancy and childhood, but in only one of these was the diagnosis of congenital syphilis made before death. It was found to be a cause of asphyxia neonatorum and unexplained sudden death in infants and should be borne in mind as a cause of non-development and infantilism in children and young adults.

Heart-Block

Galloway and Fenton[8] report a case of Stokes-Adams disease in a boy of 18. He had repeated fainting attacks with a pulse-rate of 32 to 40 per minute. There was no cardiac hypertrophy or evidence of valvular lesions. Pulse tracings showed the case to be one of partial heart-block, the ratio of the auricular and ventricular rhythm being usually 2 to 1, occasionally 1 to 1.

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Armstrong and Mönckeberg[9] present, respectively, the clinical and anatomic aspects of a case of heart-block in a 5-year-old boy. This case had been reported previous to the boy's death by Armstrong.[10] The patient first came under observation Aug. 3, 1909, at which time he had a high temperature and convulsions. He was first thought to have meningitis, but this was ruled out by a normal cerebrospinal fluid. The diagnosis was made from tracings of the jugular vein and radial artery which showed no relation between the auricular and ventricular systoles. Belladonna had no effect on ventricular pulse-rate. The average pulse-rate was between 40 and 50 beats per minute. The boy died July 25, 1910, in an epileptiform attack. Necropsy showed a lymphangio-endothelioma of the auriculoventricular node.

Cleveland's[11] case was a boy of 15 with attacks of unconsciousness without convulsions and a pulse-rate usually about 30 beats per minute. On one occasion the rate was counted with a stethoscope as 10 per minute. The heart was normal in size and position clinically. Autopsy showed hypertrophy of the left ventricle but no valvular disease. There was no microscopic examination of the auriculoventricular node or bundle.

Fulton, Judson and Norris[12] report three cases of heart-block in the same family, the father, 41 years old, a daughter 20 years old and an infant 22 months old. Pulse-tracings from all showed incoordination between the auricles and ventricles. They conclude that the most reasonable hypothesis is a congenital physiologic and perhaps anatomic abnormality in the auriculoventricular bundle or its blood-supply.

Two cases of heart-block in diphtheria have been recently reported. Magnus-Alsleben[13] has reported a case of complete heart-block in diphtheria in a child, aged 8 years, in which microscopic examination of the auriculoventricular bundle showed a severe parenchymatous degeneration.

Fleming and Kennedy's[14] case was a girl aged 10. On the sixth day of illness there was a marked variation in the pulse-rate between 40 and 88 per minute; on the eighth day there was evidence of cardiac dilatation; on the ninth day there was palatal paralysis; on the tenth day of the illness she died. Tracings showed the auricles and ventricles beating at different rates. The auriculoventricular node and the first part of the auriculoventricular bundle showed a well-marked acute inflammatory condition. The muscle of the auricles and ventricles showed myocarditis. The vagi showed no changes. These cases show that a slow pulse in diphtheria is not necessarily the result of inhibitory cardiac impulses.

Endocarditis, Myocarditis and Pericarditis

Poynton[15] includes tachycardia as one of rarer occurrences in the rheumatism of childhood. It occurs more frequently with mitral stenosis than with any other lesion and may be paroxysmal or persistent. Tachycardia is common when the myocardium suffers out of proportion to the valves. He has never seen a case associated with exophthalmic goiter and hesitates to ascribe early persistent tachycardia to any disturbance of the thyroid.

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[9] Armstrong, H., and Mönckeberg, J. G.: Herzblock, bedingt durch primären Herztumor bei einem 5-jährigen Kinde, Deutsch. Arch. f. klin. Med., 1911, cii, 1-2, 144.

[10] Armstrong, H.: A Case of Stokes-Adams Disease in a Boy Aged Five, Liverpool M.-chir. Jour., 1910, xxx, 58, 327.

[11] Cleveland, A. J.: A Case of Stokes-Adams Disease in a Boy, Aged Fifteen Years, Brit. Jour. Child. Dis., May, 1911, viii, 80, 209.

[12] Fulton, Z. M. K., Judson, C. F., and Norris, G. W.: Congenital Heart-Block Occurring in a Father and Two Children, One an Infant, Am. Jour. Med. Sc., September, 1910, cxl, 339.

[13] Magnus-Alsleben, E.: Zur Kenntnis der vorübergehenden Ueberleitungsstörungen des Herzens, Ztschr. f. klin. Med., 1910, lxix, 82.

[14] Fleming, G. B., and Kennedy, A. M.: A Case of Complete Heart-Block in Diphtheria, with an Account of Post-Mortem Findings, Heart, November, 1910. ii, 2, 77.

[15] Poynton, F. J.: Some of the Rarer Occurrences in the Rheumatism of Childhood, Brit. Med. Jour., Jan. 7, 1911, i, 5.

Wynter[16] calls attention to the fact that in pericarditis there is an absence of abdominal respiratory movements. He believes that primary thoracic disease has a share in causing suspended function of the diaphragm as well as acute abdominal conditions. When one lung or pleura is affected the influence on abdominal movement is less marked. In acute pericarditis, on the other hand, the cessation of phrenic action is bilateral. Consequently, absence of abdominal movement is as obvious as in acute abdominal disorders, although other abdominal manifestations, such as muscular rigidity and general tenderness are lacking. X-ray examination shows the diaphragm to be inert. Restriction of abdominal movement is more marked in fibrinous pericarditis than in pericarditis with effusion. It is absent in adherent pericardium. Wynter reports twelve cases in children and in adults.

Cockayne[17] examined the records of 780 cases of chorea to find out what influence the salicylates had on the cardiac lesions of the disease. Out of the 780 cases he found seventy-seven which showed, while the patients were in the hospital, clinical evidence of the onset of endocarditis, myocarditis or pericarditis and also evidence of a fresh lighting up of an acute rheumatic process in the heart. Of the seventy-seven cases thirty-nine were not treated and thirty-eight were treated with salicylates. Of the 780 cases, 355 patients were given salicylates and 425 received other treatment. If the drug had no effect the numbers showing cardiac change should be in the proportion of thirty-nine untreated to thirty-two treated with salicylates, and the actual numbers obtained are so near these that the disparity can have no significance. The statistics do not show that large doses have any more effect in preventing the progress of cardiac trouble than small ones, although the number of cases in which large doses were given was small. He concludes that the organisms of rheumatism were probably present in the myocardium, endocardium or pericardium in these cases, and the salicylates (in the doses usually given) appear to have no action in preventing their entrance into the heart, nor in stopping their further activity when once established there.

Nobécourt and Voisin[18] maintain that an accurate study of the relative cardiac dulness is of great aid in making clear the diagnosis, prognosis and treatment of heart disease in children. They computed the surface area of the heart by the formula of Potain. The product of the vertical diameter, measured in centimeters from the superior border of liver dulness to the top of the cardiac dulness, the line measured being parallel to the median line; and the horizontal diameter of the heart measured in centimeters from the junction of the right border of cardiac dulness and the upper border of the liver to the apex, this line not necessarily being horizontal; multiplied by the constant .83. They studied in all thirty-six cases. Two cases of congenital heart disease showed a formula a little above normal; two cases of adherent pericardium showed a formula a little or not at all increased. A fixed apex with a diminished area of dulness they believe to be certain evidence of adherent pericardium. From a study of twelve cases of acute cardiopathy they conclude that (1) there exists an increase of precordial dulness without any sign of endo- or pericarditis; (2) the modifications of the precordial dulness coincident with an acute endocarditis are very marked; (3) in pericarditis the modifications are still more important. In the remaining cases, twenty in number, the cardiac condition was chronic. Compensated mitral insuf-

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16. Wynter, W. Essex: Absence of Abdominal Respiratory Movement as an Indication of Pericarditis, Proc. Roy. Soc. Med., February, 1911, iv, 4, 40.

17. Cockayne, E. A.: The Influence of Salicylates on the Cardiac Lesions of Chorea, Quart. Jour. Med., April, 1911, iv, 15, 336.

18. Nobécourt, P., and Voisin, R.: La Matité précordiale dans les cardiopathies Infantiles, Arch. d. mal. du Cœur, February, 1911, iv, 2, 65.

ficiency shows only a slight increase in the surface area but the onset of an acute process is quickly seen by the increased formula. The manner in which changes in this surface area of the heart would influence prognosis and treatment is evident.

McKenzie[19] states that the prognosis of pneumonia is influenced not only by chemical processes, but also by mechanical ones. Changes in the shape and size of the heart, when the vascular system is otherwise normal, may be due to extensive collapse of the pulmonary tissue and rickety deformity of the chest wall, both throwing extra work on the right ventricle. The mechanical effect of rickety deformities he explains as follows: These deformities are over one of the most expansile parts of the lung, expansion is hindered and respiration becomes chiefly diaphragmatic, the pumping action of the expanding and contracting lung is partially lost and consequently more work falls on the right ventricle.

Stoerk[20] reports a case of dextrocardia in a boy aged 11 who came to the hospital because of a left-sided paralysis. There were no cardiac symptoms except that after running he was more easily tired than other children and had palpitation, which he localized to the right of the median line. The heart showed marked mobility on change of position from one side to the other.

Arteries and Veins

Hallé and Schreiber[21] after a brief review of ten similar cases previously reported, present a case of aortic aneurism in a boy aged 5. The diagnosis was confirmed by *x*-ray examination. The etiology of the condition was absolutely unknown. The Wassermann reaction was negative.

Coombs[22] found in 51 per cent. of 100 consecutive patients between 3 and 15 years of age, a venous hum, continuous through systole and diastole, immediately below the sternoclavicular joint or joints. This murmur was accentuated at the beginning of systole and diastole, was more common on the right side, best heard when the head was retracted and usually absent in the recumbent position. It is produced in the jugular veins but it is not clear by what mechanism. Though associated with anemia it may occur in perfectly healthy children. It is not especially associated with tuberculosis or any enlargement of the intrathoracic lymph-glands and has no diagnostic value.

Among the rarer occurrences in the rheumatism of childhood Poynton[18] includes venous thrombosis. In all the cases he has seen there was severe heart disease and only two patients survived. All cases have been of the large veins of the neck and upper extremities. When the large veins of the neck are involved the sudden edema may be mistaken for parotitis. It is a question whether this thrombosis is due to a mechanical or to a rheumatic lesion.

Hamburger[23] has frequently noticed that the arteries, especially the radials and temporals, in children after the sixth or seventh year are very easily palpable. This is not due to sclerotic changes or renal disease but, he believes, to increased arterial tonus due to vasomotor influences. This arterial rigidity is most commonly found during the school age in nervous children who often complain of headache and palpitation of the heart and other symptoms of increased vasomotor irritability.

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[19] McKenzie, I.: On the Interdependence of the Circulatory and Respiratory Systems, Brit. Med. Jour., April 22, 1911, i, 927.

[20] Stoerk, E.: Ein Beitrag zur Frage der Dextrocardie, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh., Wien, 1911, x, 2, 12.

[21] Hallé, J., and Schreiber, H.: Ectasie Aortique chez un Enfant, Arch. d. mal. des enf., August, 1911, xiv, 8, 603.

[22] Coombs, C.: The Venous Murmurs Heard at the Root of the Neck in Children, Brit. Jour. Child. Dis., March, 1911, viii, 87, 109.

[23] Hamburger, F.: Ueber Arterienrigidität im Kindesalter, München. med. Wchnschr., Jan. 31, 1911, lviii, 5, 250.

GENITO-URINARY SYSTEM

Recent Contributions to Our Knowledge of the Diseases of the Kidney

KIDNEY METABOLISM

Frey[1] has investigated the method of urine formation by a study of the freezing point and sodium chlorid concentration in the urine as compared with blood-serum. He first determined the relations under normal conditions and then the relations under diuresis. Phloridzin produces a diuresis without widening of the vessels of the kidney, and is therefore a tubular diuresis. The resulting urine does not become more like blood-serum than before. So he concludes that the urine formation in the tubules is a secretion. When caffein or the nitrites are given, which produce a constriction and dilatation of the vessels, the resulting urine always approaches in character that of the blood-serum. This is a glomerular diuresis and he therefore concludes that the product of the glomerulus is a filtration of the blood-serum. NaCl is a filtration product. Urine formation is dependent largely on the action of the tubules by which the filtration products of the glomeruli are exchanged for other constituents. All the salts except NaCl are secreted by exchange. Always some NaCl is retained in the tissues. The concentration of the NaCl in the urine regulates the amount of water excreted.

L. d'Amato and V. Faggella[2] studied the variation in NaCl, nitrogen and water excretion under forced feeding. Rabbits with an excess of urea in the diet showed an increasing excretion of nitrogen but this excreted nitrogen never equaled the amount taken in. With this increasing excretion of N there was a distinct disturbance of the chlorin balance and great variations in the water output of the kidneys. If the rabbits were given large amounts of NaCl the excretion of that substance in the urine showed great fluctuations, but the whole amount taken into the body was disposed of in a short time. The water excretion quickly returned to normal after some fluctuation. There was a distinct tendency to accumulate N. If the NaCl was given subcutaneously the retention of water with subsequent edema was easier; but this change was only temporary. If distilled water was given the water excretion was increased, with large fluctuations, and there was a loss of N and NaCl. From these experiments he concludes that a healthy kidney can get rid of an excess of water and chlorin better than an excess of urea. He believes that the depression of function after overwork is due to temporary fatigue.

The relation of the NaCl metabolism to kidney function has been shown by the work of v. Hoesslin and Kashiwado[3] to be very complicated. They mention the fact that there may be no NaCl retention in cases of kidney injury due to high temperature and to the excretion of toxins. Where there is water retention in these conditions there may be secondary NaCl retention also, which may account for the decreased NaCl secretion often found on urinalysis. They made experiments similar to those of d'Amato and found N disturbance as well as NaCl disturbance following the subcutaneous injection of NaCl. They do not think our knowledge of the action of the vasodilators on the vessels of the kidneys is sufficiently accurate to be of any value as a basis for conclusions. They also tried experiments with a mixture of yohimbin, urethane and alcohol in addition to the nitrites. Changes in the vessels, not sufficient to show in blood-pressure, did nevertheless show in the NaCl excretion. Blood-letting and compression of the trachea were also found to influence the NaCl retention. They do not believe that any conclusion based on the theory that N and NaCl behave differently because excreted in different places is sound. This is contrary to the findings of most investigators. Karsner[4] and Frey[1] believe that water and inorganic salts

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1. Frey: Deutsch. med. Wchnschr., 1911, xxxvii, 1072.
2. d'Amato and Faggella: Ztschr. f. klin. Med., 1911, lxxii, 474.
3. Von Hoesslin and Kashiwado: Deutsch. Arch. f. klin. Med., 1911, cii, 520.
4. Karsner: Jour. Am. Med. Assn., 1911, lvi, 1452.

are due to the action of the glomeruli and organic substances due to the action of the tubules.

Schlayer[5] has emphasized the importance of vascular changes in nephritis, even though the changes may not show as anatomic lesions. These always show themselves in a disturbance in water secretions—sometimes oliguria, sometimes polyuria. After a study of salt, water, iodin and sugar excretion he comes to the conclusion that the injury to the vessels does not affect the NaCl excretion. This agrees with the work of Monakow.[6] The latter author, however, does not agree that iodin and NaCl disturbances go together. He found great variation in this respect between different patients and between the same patient at different times. The N elimination is also variable and not in relation to the other elements of the urine. He would divide all cases of nephritis into groups according to their functional capacity and treat them on this basis. From a study of nine cases made during life and examined post mortem he concludes that the elimination of N is affected by the glomeruli and that NaCl and water are excreted by the tubules. If, antemortem, there was a marked disturbance of iodin excretion and no disturbance of NaCl excretion, the injury to the tubules was slight.

FUNCTION TESTS

Heitz-Boyer and Moreno[7] argue that the maximum concentration of the urine is the real test of kidney sufficiency for, since the water can be drawn from the reserves in the body, the important question is the per cent. of solid constituents. The actual amount of solids depends on the diet, but the concentration depends on the state of kidney parenchyma. A patient with nephritis fed on an excess of urea was found to eliminate a smaller per cent. of urea in his urine than a healthy individual. Ambard and Moreno[8] have worked out a very complicated formula to determine kidney sufficiency based on the facts referred to above. The proportion of urea in the blood, and the urea in the urine, together with the body weight and urine concentration, are found to bear certain definite relations in health and disease. Schlayer[5] does not believe that the urine concentration is of such great value as these authors maintain.

Geraghty and Rowntree[9] report further use of phenolsulphonephthalein in the test of kidney function. They maintain, as in previous communications, that this test is simple, accurate and valuable as an aid to prognosis and treatment. Its chief value thus far has been in surgical cases but some cases of chronic nephritis have been examined. If there is marked decrease in phthalein output, marked renal changes are present and when phthalein is excreted in very small amounts a grave prognosis should be given. Keyes[10] believes this is a valuable test as applied to surgical cases. Thomas[11] has written at length concerning the use of indigo-carmin as a test of kidney function as applied especially to surgical conditions. Roth[12] has found the method unsatisfactory except in cases of renal calculi.

TREATMENT

Vogel[13] emphasizes the importance from a therapeutic standpoint of the study of NaCl and water elimination. He gives a list of the NaCl content of the various food-stuffs. Hürter[14] also gives a carefully prepared list of foods with their protein and salt content, together with their caloric values. This article by

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[5] Schlayer: Deutsch. Arch. f. klin. Med., 1911, cii, 311.

[6] Monakow: Deutsch. Arch. f. klin. Med., 1911, cii, 248.

[7] Heitz-Boyer and Moreno: Presse méd., 1911, xix, 245.

[8] Ambard and Moreno: Semaine méd., 1911, xxxi, 181.

[9] Geraghty and Rowntree: Jour. Am. Med. Assn., 1911, lvii, 811.

[10] Keyes: Am. Jour. Urol., 1911, vii, 125.

[11] Thomas: Surg., Gyn. and Obst., 1911, xii, 345.

[12] Roth: Ztschr. f. Urol., 1911, v, 439.

[13] Vogel: Arch. Int. Med., 1911, vii, 602.

[14] Hürter: Med. Klin., 1911, vii, 55.

Hürter is an excellent review of our present knowledge of the rationale of the treatment of acute nephritis and of the details to be employed in the carrying out of that treatment. Karsner[4] has presented the subject from the chemical side with the same cleanness and precision.

Fischer[15] has advocated a method of treatment somewhat different from the usual one based on his contention that the underlying cause of every nephritis is an abnormal production or accumulation of acid by the kidney. On this basis he would explain the abnormal cloudy swelling of the kidney and also the formation of casts. The disturbances of water secretion are due, he believes, to the effects of the acid in interfering with the normal production and loss of carbon dioxid in the parenchyma of the kidney. The change in the other elements in the urine, he believes, are due to the effect of the acid in changing the absorption properties of the kidney colloids.

The treatment of nephritis on this basis is to avoid all conditions which favor an abnormal accumulation or production of acid in the kidney. Water is not restricted. The only danger from giving water is the washing out of salts which may thus favor the action of acids. This danger is avoided by giving salts in the diet, including NaCl. The giving of alkalies is also recommended. Francis[16] also advises the use of sodium carbonate in nephritis and the use of lime water by rectum. Levenson[17] advocates the use of potassium acetate or nitrate to favor the elimination of chlorids but adds that it is of doubtful value in nephritic œdema.

Bonnarnour, Imbert and Jourdan[18] and Vitry[19] advise the use of calcium chlorid as a diuretic in nephritis. It does not influence the albumin, but distinctly increases the water output.

UREMIA

Obermayer and Popper[20] contend that the presence of indican in the blood-serum is of great importance in the diagnosis of uremia. They have reviewed the literature carefully and added a number of their own cases. With the indicanemia there is also N retention and molecular contraction of the blood.

Tyson[21] advocates the more frequent use of nephrotomy in chronic nephritis and gives as the indications, permanent dropsy, uremia, anuria and large albuminuria. It should be used, however, only after medical treatment is unavailing. The operation is contraindicated in patients with valvular heart disease or albuminuric retinitis. The benefit comes from the relief of tension, with possibly some stimulation of the blood-supply between the organ and the surrounding tissue. La Rogue[22] agrees substantially with all these contentions.

Gumbel[23] points out that the beneficial results from this operation are of course only in the relief of symptoms and not in any healing of the damaged kidney. He reports a case of a girl of 6 years operated on with good results.

Zondek[24] argues that if the benefit is largely due to relief of tension, scarification would be as valuable as capsule-stripping. He found from experiments in animals that more bleeding resulted from multiple incisions of the capsule than from the ordinary operation; therefore he recommends this procedure.

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15. Fischer: Jour. Am. Med. Assn., 1911, lvii, 149.
16. Francis: Med. Herald, 1910, xxix, 133.
17. Levenson: Jour. Am. Med. Assn., 1911, lvii, 150.
18. Bonnarnour, Imbert and Jourdan: Lyon méd., 1911, cxvi, 148.
19. Vitry: Presse méd., 1911, lxi, 633.
20. Obermayer and Popper: Ztschr. f. klin. Med., 1911, lxxii, 332.
21. Tyson: Med. Rec., New York, 1911, lxxx, 57.
22. La Rogue: Virginia Med. Semi-Monthly, 1911, xv, 505.
23. Gumbel: Deutsch. med. Wchnschr., 1911, xxxvii, 594.
24. Zondeck: Berl. klin. Wchnschr., 1911, xlviii, 571.

ETIOLOGY

Fischer's[15] belief in regard to the cause of nephritis has already been mentioned. Other statements (Blumer,[25] Weitlander[26]) confirm the common belief that nephritis is usually a secondary manifestation of some infection, though cases like those reported by Marfan[27] are common in which no etiologic factor can be determined. No progress has been made in this direction.

EXOPHTHALMOS

Gordinier[28] and Mitchell[29] have both drawn attention to the presence of exophthalmos in connection with chronic nephritis—the nephritis occurring spontaneously in man or produced experimentally in animals. This is believed to be connected in some way with the presence of toxins in the blood, due to renal insufficiency, which act on the sympathetic nervous system.

BLOOD-PRESSURE

Gordon[30] found that the blood-pressure in acute nephritis in children was frequently elevated and highest in those cases which showed blood and slight edema.

ANEMIA

Pribram[31] believes that the anemia of chronic nephritis is due to overaction of the adrenals, due to stimulation by toxins retained by the diseased kidney.

URINALYSIS

Albumose can be detected by the test of Fittipaldi[32] which consists in dissolving the alcoholic precipitate of urine in 31 to 32 per cent. soda solution and adding a few drops of this to a 5 per cent. solution of equal parts of nickel sulphate and ammonia. An orange-yellow color indicates the presence of albumose. The occurrence of albumin in the urine does not interfere with the test.

To detect small quantities of albumin Glaesgen[33] suggests always using a control specimen of urine. He advocates boiling the urine after adding a few drops of 20 per cent. acetic acid as the method which is most reliable. Katzenstein[34] always uses the rays of light passed through the urine at right angles to the line of vision as a means of detecting small amounts of albumin and as a method of especial use at night. J. B. Smith[35] has called attention to a method of detecting sugar and urates by measuring the amount of heat generated in a given time after the addition of potassium permanganate; also a method of determining the total nitrogen—too complicated for clinical use. Barberio[36] gives a new test for the estimation of indican in the urine. The test consists in adding two or three drops of a 1 to 2,000 sodium nitrite solution to 5 c.c. of filtered urine. After shaking add 5 c.c. of a concentrated HCl and 2 c.c. of chloroform. The color of the urine changes from yellow to violet and of the chloroform to blue. This test is very easy and rapid.

Woodyatt and Helmholz[37] warn against the error in the use of charcoal as a clearing agent for urine because of the impurities in the charcoal.

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25. Blumer: Yale Med. Jour., 1911, xvii, 293.
26. Weitlander: Med. klin., 1911, vii, 735.
27. Marfan: Med. Press and Circ., 1910, xc, 644.
28. Gordinier: New York State Jour. Med., 1911, xi, 357.
29. Mitchell: Jour. Med. Research, 1911, xxiv, 69.
30. Gordon: Arch. of Pediat., 1911, xxviii, 343.
31. Pribram: München. med. Wchnschr., 1911, lviii, 1613.
32. Fittipaldi: Gazz. d. osp., 1911, xxxii, 518.
33. Glaesgen: München. med. Wchnschr., 1911, lviii, 1123.
34. Katzenstein: Jour. Am. Med. Assn., 1911, lvi, 662.
35. Smith, J. B.: Med. Press and Circ., 1911, xci, 9, 85, 117, 170.
36. Barberio: Policlinico, Rome, 1911, xviii, 517.
37. Woodyatt and Helmholz: Arch. Int. Med., 1911, vii, 598.

Pribram[38] reports the production in animals of hemolysins, precipitins and complement binding antibodies by the subcutaneous injection of urine. Notthofft[39] reports cases of red coloration of urine due to eating mushrooms.

Engel and Turnau,[40] Tugendreich[41] and Boschan[42] report that a black precipitate forms in the urine of breast-fed babies when the urine is boiled after the addition of a small amount of a 2 per cent. silver nitrate solution. This reaction is due to the reduction of the silver nitrate by the chlorids in the urine. It does not occur in bottle-fed babies.

Raudnitz[43] confined puppies in a small space with their own decomposing urine. The puppies showed no tendency toward any disease. He was led to make this experiment because of two infants with rachitis who lived very near a factory urinal.

Aufrecht[44] describes the technic for determining the amount of uric acid in the urine. Stephan[45] gives a slight modification of this. The test depends on titration against potassium permanganate of evaporated urine after the addition of ammonium chlorid or sulphate.

Baar[46] gives the results of many tests for bile and indican made in patients with gastro-intestinal diseases and patients after operation. All patients showing bile and indican in the urine have a lesion of the gastro-intestinal tract. In laparotomy there is no bile nor indican unless there is trauma to the intestinal wall. These observations may be used in differentiating functional disturbances of the gastro-intestinal tract and conditions with anatomic lesions.

ALBUMINURIA

Lury[47] experimented with 100 children whose urine was free from albumin, having them stand in lordosis. Only those with abnormally movable kidneys showed albumin in the urine as a result of the position. Piesen[48] agreed with these observations and found also that the common attitude of children—sitting with arms folded behind the back—was liable to induce albuminuria and he thought was injurious to the kidney. Hamill and Blackfan[49] studied the occurrence of albumin in the urine of healthy children and found that none of their cases could be explained on the postural basis. They believe the albumin to be due to a temporary overtaxation of the kidneys from the ordinary habits of life. Lüdke and Sturm[50] do not agree that the transient albumin in the urine is due to posture. They are inclined to connect it with some toxic condition and believe it may be of some value in differentiating the stages of tuberculosis. This belief is founded on the study of 140 tuberculous patients, in 102 of whom albumin was found in the urine.

COLLECTING URINE

Lawrence[51] describes a method of collecting urine from female infants. A piece of adhesive plaster is fastened securely over the genital region. Through an opening cut in this plaster a finger of an old rubber glove is inserted to the other end of which a test tube is attached.

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38. Pribram: Deutsch. Arch. f. klin. Med., 1911, cii, 457.
39. Notthafft, München. med. Wchnschr., 1911, lviii, 140.
40. Engel and Turnau: Berl. klin. Wchnschr., 1911, xlviii, 18.
41. Tugendreich: Berl. klin. Wchnschr., 1911, xlviii, 224.
42. Boschan: Berl. klin. Wchnschr., 1911, xlviii, 302.
43. Raudnitz: Jahrb. ɪ. Kinderh., 1911, lxxiii, 259.
44. Aufrecht: Berl. klin. Wchnschr., 1911, xlviii, 627.
45. Stephan: Berl. klin. Wchnschr., 1911, xlviii, 897.
46. Baar: Northwest Med., 1911, iii, 123.
47. Lury: Jahrb. f. Kinderh., 1910, lxii, 705.
48. Piesen: Wien. klin. Wchnschr., 1911, xxiv, 12.
49. Hamill and Blackfan: Am. Jour. Dis. Child., 1911, i, 139.
50. Lüdke and Sturm: München. med. Wchnschr., 1911, lviii, 993.
51. Lawrence: Boston Med. and Surg. Jour., 1911, clxiv, 309.

NOTE.—Other articles on the subject of nephritis are given below. These have not been quoted because they either contain nothing new or nothing with particular reference to pediatrics. No articles published earlier than January 1, 1911, have been included in this abstract.

Zorkendorfer: Wien. klin. Wchnschr., 1911, xxiv, 159.
Rosenthal: Deutsch. med. Wchnschr., 1911, xxxvii, 923.
Beiheig: Deutsch. Arch. f. klin. Med., 1911, cii, 507.
Goodman: New York Med. Jour., 1911, xciii, 777.
Fuhs and Lintz: Jour. Am. Med. Assn., 1911, lvi, 1882.
Pechstein: Ztschr. f. Kinderh., 1911, i, 356.
Fenner: New Orleans Med. and Surg. Jour., 1911, lxiii, 499.
Tirard: Clin. Jour., 1911, xxxvii, 401.
Smith, F. J.: Clin. Jour., 1911, xxxviii, 17.
Beard: Kentucky Med. Jour., 1911, ix, 120.
Thompson: Kentucky Med. Jour., 1911, ix, 115.
Autenreith and Müller: München. med. Wchnschr., 1911, lviii, 899.
Katz and Lichtenstern: Wien. klin. Wchnschr., 1911, xxiv, 811.
Nellis: New York State Jour. Med., 1911, xi, 185.
Schippers: Deutsch. Arch. f. klin. Med., 1911, ci, 543.
Moraczewski: Arch. f. Verdauungskr., 1911, xvii, 23.
Ronot: Lyon Chir., 1911, v, 615.
Marinacci: Policlinico, Rome, 1911, xviii, 145.
Pflanz: Wien. klin. Wchnschr., 1911, xxiv, 345.
Schenck: Surg., Gyn. and Obst., 1911, xiii, 68.
Simon: Ztschr. f. Kinderh., 1911, ii, 1.
Schulz: Deutsch. Arch. f. klin. Med., 1911, cii, 1.

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METABOLISM AND NUTRITION

The Rôle of the Carbohydrates in Creatin-Creatinin Metabolism

(*Lafayette B. Mendel and William C. Rose: Jour. Biol. Chem., 1911, x, 213*)

Two fundamental facts are emphasized by the experiments of Mendel and Rose: (1) An increase in the elimination of total creatinin (i. e., creatin plus creatinin) is always accompanied by an increase in the output of total nitrogen; and (2) carbohydrates, in contrast to the other food-stuffs, are capable of preventing the excretion of creatin and are therefore indispensable for normal creatin-creatinin metabolism. They found that the excretion of creatin induced by starvation, is inhibited in rabbits by feeding a diet of carbohydrates absolutely free from proteins and fats. When the carbohydrates are given in liberal amounts, creatin entirely disappears from the urine. The creatin elimination is not reduced by feeding a diet of fat alone, or by a diet of fat and protein. Experimental interference with carbohydrate metabolism leads to the elimination of creatin. After phloridzin diabetes which depletes the store of carbohydrates and during phosphorus poisoning, which disturbs the glycogenic functions, the output of creatin in dogs is decidedly increased. An increase in the output of creatin plus creatinin (total creatinin), is always accompanied by an increase in total nitrogen elimination. This parellelism of total creatinin and total nitrogen outputs in inanition and with nitrogen-free diets is ascribed to a common source, namely, true tissue or endogenous metabolism. The metabolism of exogenous or reserve proteins is not accompanied by the production of creatin or creatinin. The intimate relation of creatin excretion (or the failure of conversion into creatinin) to carbohydrate metabolism, is discussed in detail.

Excretion of Creatin in Infancy and Childhood

(*William C. Rose: Jour. Biol. Chem., 1911, x, 265*)

In view of the observations that creatin is a normal constituent of the urine of sucklings, Rose attempted to determine the age at which this product disappeared. Thirty-nine specimens of urine from children of different ages were analyzed. With the exception of two cases, creatin was present in all specimens from children under fifteen years of age. A boy of ten and a girl of thirteen failed to have creatin in their urines. No progressive decrease in the percentage of the total creatinin in the form of creatin coincident with increase in age is apparent; nor is the percentage of creatin constant for the same individual. For instance, one specimen obtained from a child of five years contained 24.2 per cent. of the total creatinin in the form of creatin, while a second sample from the same child a few days later, contained 79.2 per cent. of the total creatinin as creatin. It was impossible to obtain information as to the amount and kind of food eaten by the children. Most of the specimens were obtained from the city orphan homes or from private families, and the subjects of the experiments were probably ingesting more or less meat. It is possible, therefore, that the oxidation or conversion of creatin into creatinin may be difficult for young individuals to accomplish and in this case the creatin of the urine may, in part, represent ingested creatin; or the glycogenic functions may be imperfectly developed and the store of carbohydrates be insufficient to exert its regulatory influence over metabolism during childhood.

ACUTE INFECTIOUS DISEASES

Poliomyelitis

(*H. W. Hill: Tr. A. M. A., Sec. Prev. Med., 1910*)

In a statistical study of poliomyelitis in Minnesota by Hill, including cases that showed no paralysis, the maximum number available for his purposes was 333, which he estimates as something more than one-third of the total number occurring in the state. The majority of the cases occurred in the cities of St. Paul, St. Peter, and one or two other towns. Of the epidemiologic points, abortive cases, contagiousness, and mortality are the chief, and to these he gives the most attention. He admits certain shortcomings in his studies but finds, so far as the figures elsewhere are available, that they generally correspond with his own. As regards contagion, he does not find evidence that direct transmission of the disease from one person to another occurs with sufficient frequency to be of great importance. Dust, he believes, is an element of serious consequence and explains the high rural typical cases, and the spread by abortive cases, he thinks, would be even less probable. The same would also be true of carriers of incidence in children and in males at all ages. No other infectious disease is so influenced by dust-laying rainfall, and this suggests a possibility in the treatment of epidemics. Horses, especially farm horses, associate together on market days, etc., as much as their owners, and a disease clinically like poliomyelitis has existed in colts in Minnesota for some years and has been observed, though not recognized, by veterinarians all over the state and also in North Dakota. The intestinal discharges in horses are almost ubiquitous in street dust and also on country roads, and in the neighborhoods of isolated farm houses. They are sufficiently massive to protect imbedded organisms from direct sunlight and drying, yet pulverize readily, especially under heavy traffic, and may be easily blown about or tracked into houses, particularly in rural communities. It seems to him impossible that the infecting agent can be derived from the discharges of human beings, as in that part of the country they are not mixed with the ordinary dust. While in the South this is more likely, poliomyelitis has not been especially prevalent there. Hill offers this as a working hypothesis for further investigation. Numerous tables accompany the article, covering nearly all the conditions and relations of the disease.

TUBERCULOSIS AND SYPHILIS

Inherited Syphilis

(*C. S. Bull: Paper prepared for but not read in Sect. on Opht. A. M. A., 1910*)

C. S. Bull, New York, calls special attention to the early recognition of the stigmata of hereditary syphilis in infants and very young children. One of the greatest of social dangers is the high rate of infant mortality in the children of syphilitic parents, but a greater one is the disastrous one of heredity in those who live to maturity. In many cases of inherited ocular syphilis the lesions are so ill defined as to be unrecognizable except by the expert observer. Hence the examination should begin with the new-born infant and should be repeated at brief intervals through early childhood to youth. It is a mistake to suppose that congenital syphilitic lesions of the eye run a mild course, and he points out how lesions of the uveal tract frequently escape casual observation, though they can usually be recognized with care, because at this early age a coexisting keratitis is rare. The prognosis as to vision is largely influenced by the coexistence of other ocular stigmata. As most of these children die early, proper tests of vision often cannot be made. When the disease occurs later in child life, he is inclined to think the retina suffers less, but if retinitis or optic neuritis occur the end is, in his experience, partial or complete atrophy. He has noted the coincidence of interstitial keratitis and a vertically oval cornea occurring frequently in these cases for years, and Fuchs has recently called attention to it (*Ophthalmic Rev.*, September, 1909). If such malformation exists careful scrutiny will often reveal faint traces of former interstitial keratitis. Taken alone, however, it cannot be considered as absolute proof of inherited syphilis. As he is speaking of young children before the eruption of the permanent teeth, the dental stigmata cannot give much assistance, but the ears should be carefully examined. Pain, inflammation or discharge from the ears in infancy will often reveal scars of early trouble. If these are not found the hearing should be tested for functional disturbance, but much cannot be expected from these tests. There is a variety of aural trouble without appreciable lesion which is known to be due to inherited syphilis. This is the *surdite foudroyante* characterized by a sudden invasion, rapidity and severity of course and ending in a total loss of hearing in a few days or hours. Naturally from this occurring in early childhood there are defects in speech varying in degree to actual mutism. Facial stigmata are often accompanying the ocular or aural symptoms, and there are certain phenomena of first dentition strongly suggestive of inherited syphilis, such as very small size of the incisor teeth and the persistence and permanence of the first teeth beyond the usual period. In conclusion, he quotes Fournier's therapeutic deduction as to the necessity of specific treatment of the child or parents when the stigmata are present, and he is inclined to add to them a recommendation of sterilization of parents producing children with these stigmata.

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INFANTILE PARALYSIS

WITH ESPECIAL REFERENCE TO ITS OCCURRENCE IN MASSACHUSETTS, 1907-1910 *

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BOSTON

The problem of infantile paralysis is definitely before the physicians of the United States.

In the twenty years from 1881 to 1900 there were reported in this country 200 cases. In the five-year period beginning in 1900 and ending in 1904 there were reported 100 cases. In the five years beginning in 1905 and ending in 1909, 5,400 cases, and in one — the year 1910 — approximately 9,000 cases. Such an extraordinary increase, in which Europe has in no way shared, brings before us very seriously our obligation to investigate the disease, to take account of our stock of knowledge regarding it and to do what we properly can do to quiet the panic that exists in the minds of the laity, by placing before them what we know and by asking their assistance to help us to learn more (Charts 1, 2 and 3).

The present paper will consist of a brief résumé of our present accepted knowledge of the various aspects of the disease and an analysis of the studies in Massachusetts made by the State Board of Health for the four years beginning in 1907.

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*Read at the Los Angeles Session of the American Medical Association, at a joint session of the Section on Practice of Medicine and the Section on Diseases of Children, June , 1911.

*This paper was prepared with the co-operation of Henry P. Walcott, M.D., Chairman of the Massachusetts State Board of Health, and of Theobald Smith, M.D., Milton J. Rosenau, M.D., John Lovett Morse, M.D., and James H. Wright, M.D., Advisory Committee on Infantile Paralysis to the Massachusetts State Board of Health.

In the field work the Board has had for two years (1909-1910) the services of Dr. Philip A. E. Sheppard of Boston, and Dr. Thomas P. Hennelly, now of Pittsfield, Mass. The epidemic in the Deerfield Valley in 1908 was investigated by Dr. Herbert P. Emerson, of Springfield, then State Inspector of Health for that district. Much valuable assistance has been rendered furthermore by the other State Inspectors of Health throughout the Commonwealth.

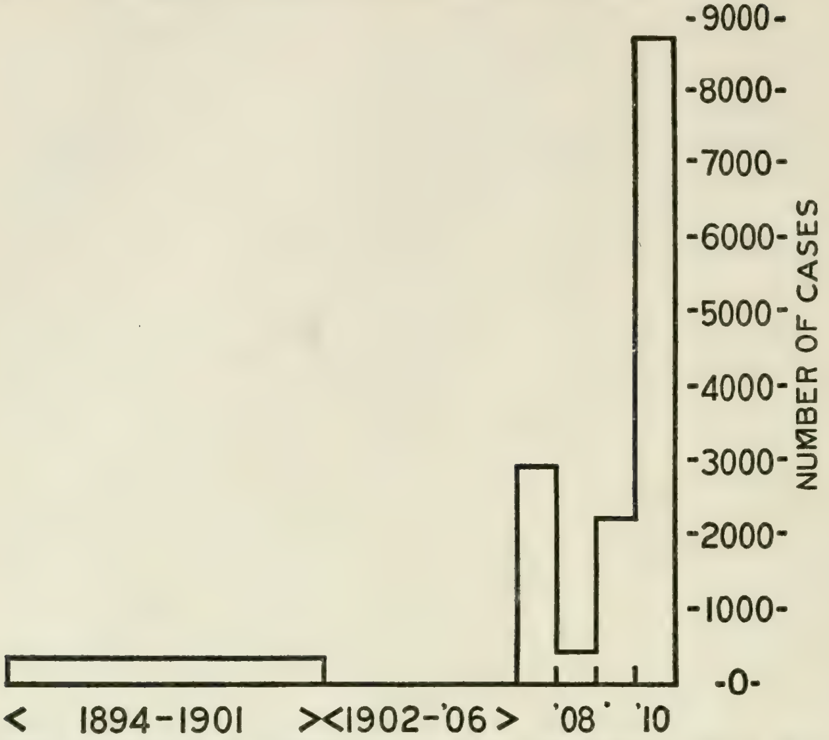

Chart 1.—Prevalence of infantile paralysis in the United States, 1894 to 1910.

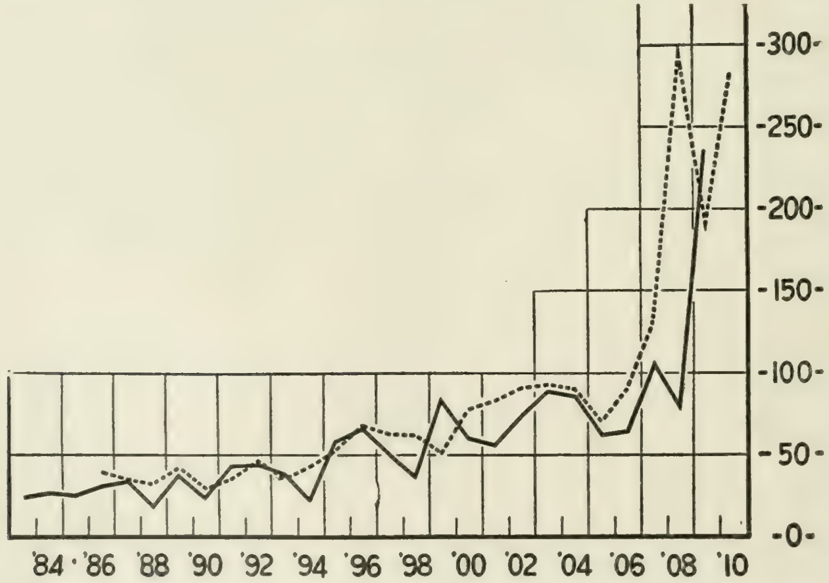

Chart 2.—Number of new patients with infantile paralysis treated at Children's Hospital, Boston, indicated by the solid black line; those treated at the New York Orthopedic Dispensary and Hospital by the dotted line; both by years.

I. RECENT HISTORY AND ETIOLOGY OF INFANTILE PARALYSIS
RÉSUMÉ OF PRESENT ACCEPTED KNOWLEDGE

History.—The disease is not a new one. Although the first clear description of it was given in 1840 by Heine, a German, it was fairly well described by an English physician, Michael Underwood, in 1774. Since the perfectly clear description of the disease by Heine, in 1840, successive additions to our knowledge have been made, the most important contributions until very recently having been by Norwegian and Swedish authors, who had unusual opportunities for the study of the disease between 1899 and 1907.

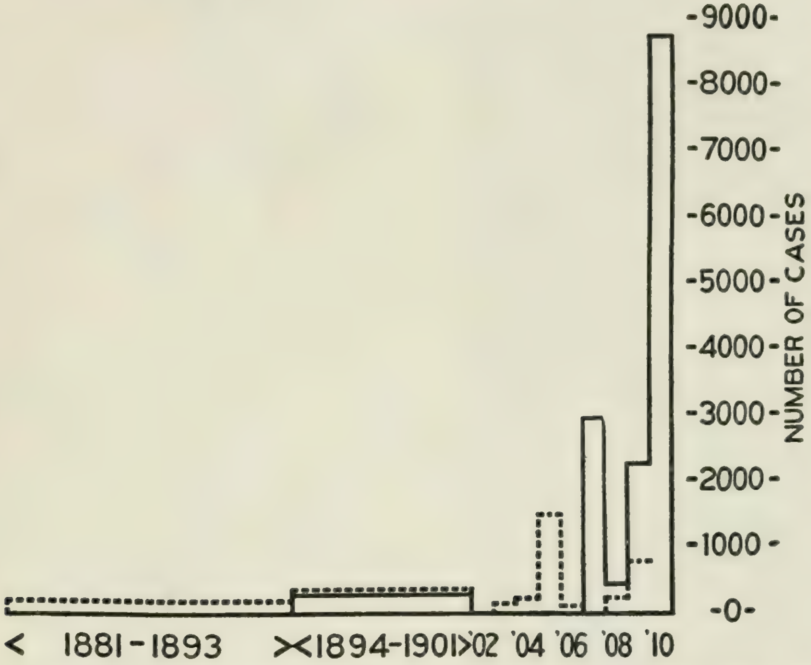

Chart 3.—Relative prevalence of infantile paralysis in the United States and Europe and Australia; the solid black line refers to the United States; the dotted line to the following countries: Italy, Sweden, Norway, Germany, Austria, France, England and Australia.

Infectious Character.—Although it had long been suspected to be an infectious disease, this fact was not absolutely proved until November, 1909, when Flexner and Lewis of the Rockefeller Institute in New York demonstrated, by inoculation of a series of monkeys with tissues from children dying of the disease, that the process was an infectious one, placing it in the category with rabies, yellow fever and foot-and-mouth disease. This discovery was undoubtedly the most important addition to our knowledge of the disease ever made.

Epidemic Character.—That the disease was infectious was suggested by the fact, recognized as early as 1881, that it occurred in epidemics. Indeed, a questionable epidemic was reported in 1841 by a Louisiana physician. From 1881 until the present time, epidemics have been reported with increasing frequency, and since 1905 the size of epidemics has largely increased. We must remember, however, that of late greater attention has been paid to the disease and a larger number of cases has been recognized, so that the increase is in a measure apparent. Nevertheless, the increase has been too great to be accounted for by any theory of increased attention to the disease.

Epidemic History.—The first great epidemic of modern times occurred in Norway and Sweden in 1905, 2,000 cases being reported in Norway and Sweden together. In 1907 the first great American epidemic occurred, 2,500 cases being reported in and about New York, since which time the disease has been increasing irregularly in the United States, making a very great increase in 1910 over any previous record.

Infantile paralysis first appeared in the United States to any considerable extent in 1894, when Caverly of Rutland reported 132 cases in the Otter Creek Valley, Vermont. Some ten small epidemics were reported in the United States during the next twelve years, and in 1907 the largest epidemic on record, that in New York, occurred, some 2,900 cases having been reported in that year. In 1908 the disease was apparently quiescent, only 392 cases being reported in the United States. This was followed by outbreaks in 1909 in various parts of the country, and in Cuba for the first time, with a total for the year of 2,343 cases in all.

In 1910 the disease assumed much more serious proportions and was present in forty-three states. Several states had epidemics, 500 or more cases occurring in the District of Columbia, Iowa, Massachusetts, Minnesota, Indiana and Pennsylvania, and from 200 to 500 in Kansas, Maryland, New Hampshire, New York, Rhode Island, Virginia, Washington and Wisconsin (Chart 4).

The reasons for this marked increase in the occurrence of infantile paralysis are not clear, but certain considerations are of interest and possibly of importance.

Question of Importation.—No explanation has been given for the sudden increase of the disease in Norway and Sweden in 1905, but after that epidemic it seems not unreasonable to suppose that the disease may have been increased in this country by Scandinavian immigrants, who arrived to the number of about 42,000 in the year 1907. The epidemic of 1907 in New York may have had its origin in this way, and the disease may have been carried in a similar manner to the middle west, but the explanation is not wholly satisfactory, inasmuch as the outbreak of the disease in the west did not conform closely to the distribution of Scandi-

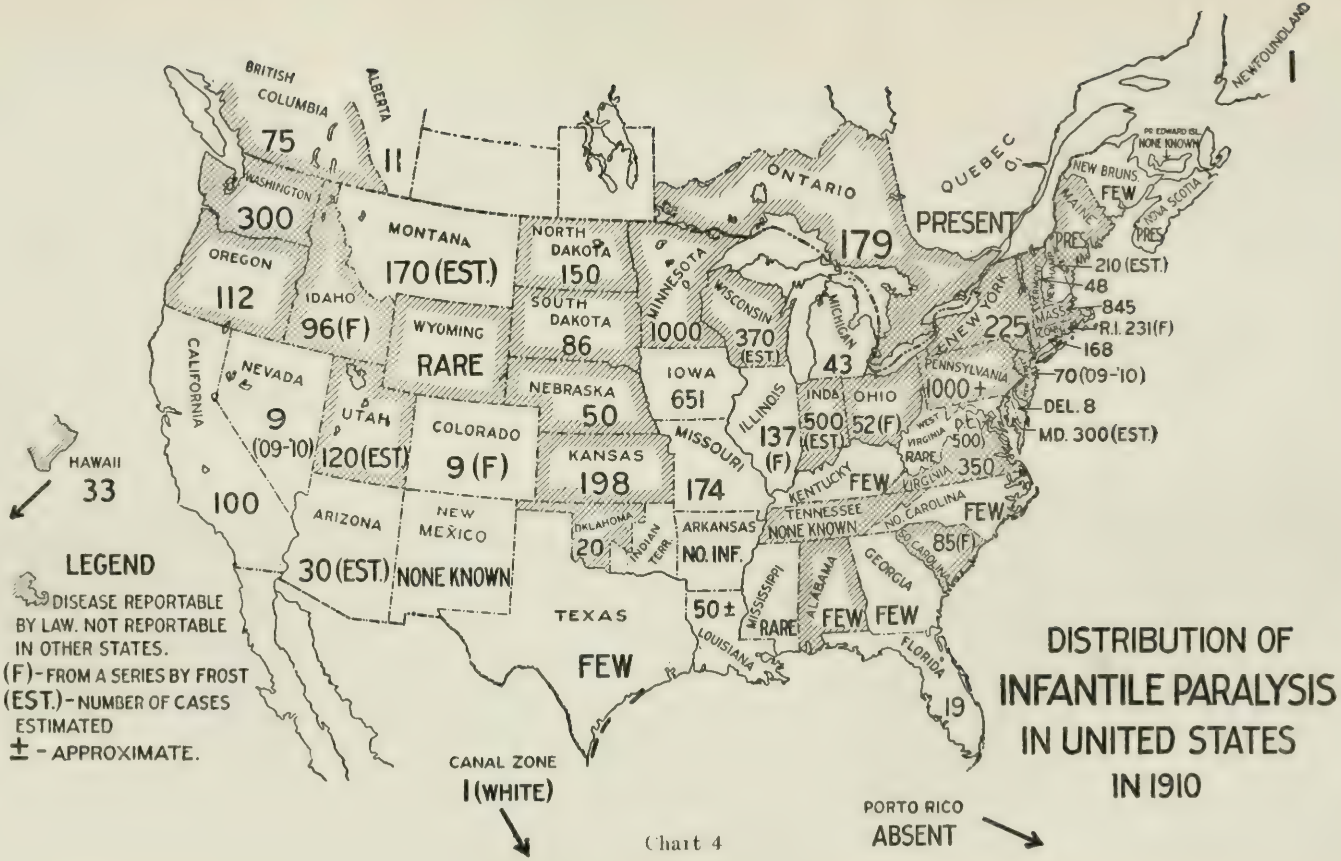
DISTRIBUTION OF
INFANTILE PARALYSIS
IN UNITED STATES
IN 1910
LEGEND
DISEASE REPORTABLE BY LAW. NOT REPORTABLE IN OTHER STATES.
(F)-FROM A SERIES BY FROST
(EST.)-NUMBER OF CASES ESTIMATED
± - APPROXIMATE.
BRITISH COLUMBIA
75
ALBERTA
11
WASHINGTON
300
OREGON
112
CALIFORNIA
100
NEVADA
9
(09-10)
IDAHO
96(F)
MONTANA
170(EST.)
WYOMING
RARE
UTAH
120(EST.)
ARIZONA
30(EST.)
COLORADO
9 (F)
NEW MEXICO
NONE KNOWN
NORTH DAKOTA
150
SOUTH DAKOTA
86
NEBRASKA
50
KANSAS
198
OKLAHOMA
20
INDIAN TERR.
TEXAS
FEW
MINNESOTA
1000
IOWA
651
MISSOURI
174
ARKANSAS
NO. INF.
LOUISIANA
50±
WISCONSIN
370
(EST.)
ILLINOIS
137
(F)
MICHIGAN
43
INDA
500
(EST.)
OHIO
52(F)
KENTUCKY
FEW
TENNESSEE
NONE KNOWN
MISSISSIPPI
RARE
ALABAMA
FEW
GEORGIA
FEW
FLORIDA
19
SO. CAROLINA
85(F)
NO. CAROLINA
FEW
VIRGINIA
350
WEST VIRGINIA
RARE
D.C.
500
PENNSYLVANIA
1000 +
NEW YORK
225
MASS.
CONN.
PRES.
210 (EST.)
48
845
R.I. 231(F)
168
70(09-'10)
DEL. 8
MD. 300(EST.)
ONTARIO
179
QUEBEC
PRESENT
MAINE
NEW BRUNS.
FEW
PR. EDWARD ISL.
NONE KNOWN
NOVA SCOTIA
PRES.
NEWFOUNDLAND
1
HAWAII
33
CANAL ZONE
1 (WHITE)
PORTO RICO
ABSENT

Chart 4

navian immigrants. The Massachusetts epidemic can be reasonably explained on the ground that it came from New York. In fact, the New York epidemic was sufficiently large to be a possible source for the outbreaks in various parts of this country.

Travel.—It has been noted in the distribution of all epidemics that they tend to spread along the lines of greatest travel; certain figures were, therefore, analyzed with regard to passenger traffic in the United States.

Steam Railways.—In 1904 there were 715,400,000 passengers carried by the railroads, and in 1908 there were 890,000,000, the average number of passengers per train mile being in the first period forty-six, and in the second fifty-four; that is, there were 175,000,000 more passengers carried per year in 1908 than in 1904.

Electric Railways.—The only available figures with regard to electric railway traffic are those for 1902 and 1907. In 1902 the number of passengers carried was 5,536,000,000, and in 1907 it was 9,500,000,000, an increase in round numbers of 4,000,000,000, or about 75 per cent. in five years.

Automobiles.—Another important factor as regards increased travel is the automobile, and here the only figures which it has been possible to analyze are those relating to Massachusetts. In 1904 there were 4,000 automobiles registered in Massachusetts; in 1909, 24,000; that is, in the five-year period the number of automobiles increased six times.

Conclusions from Study of Travel.—These figures show a very decided increase in travel in the United States in five years, an increase wholly out of proportion to the increase in population. It is not at all unlikely that it is one factor by which the disease has been distributed over the country; and if this conclusion is applied to the year 1894 when the Rutland epidemic occurred, the increased communication by travel becomes very much more marked by comparison.

Having considered these general aspects of the disease we now come to the closer consideration of its etiology.

ETIOLOGY

The disease is an infectious one, caused by an ultramicroscopic virus which passes through the closest porcelain filters, its infectious character having been proved by the fact that it can be propagated in a second and many subsequent series of monkeys from tissues of a first series.

The virus is contained in the brain and spinal cord, the mucous membrane of the nasopharynx, in infected lymph-nodes, in the salivary glands, and, in the acute stage, in the cerebrospinal fluid and the blood.

The disease may be produced experimentally in monkeys by intracerebral, intraperitoneal, subdural, intraneural, perineural and subcutaneous injections, and by implantation in the anterior chamber of the eye. The disease has been caused also by the introduction of the virus into the stomach and intestines. Successful inoculation has been accomplished by rubbing the virus into a scarified or even a sound nasal membrane, and two observers succeeded in producing the disease by inhalation of an emulsion containing the virus and by implantation in the trachea. All investigators agree, however, that the intracranial route is the best for inoculation.

Inoculation of horses, calves, goats, pigs, doves, sheep, rats, cats, mice, chickens, guinea-pigs and dogs have proved negative, and monkeys have proved the most satisfactory animals for study. A paralysis may be experimentally produced in certain varieties of young rabbits and may be transmitted from one generation to another of rabbits and finally back to monkeys by successive inoculations.

The virulence of a suspension is not impaired by drying (to nine days), by freezing, nor by suspension in glycerin for five months, but it is killed by exposure to a temperature of from 45 to 50 C. in half an hour. It is also killed by such weak disinfectants as 1 per cent. solution of peroxid of hydrogen (perhydrol of Merck) by 1 to 500 solution of permanganate of potash, and by a powder containing menthol 0.5, salol 5, and boric acid 20.

The organism is not visible with the highest powers of the microscope and will not grow on the culture media in general use.

The disease in monkeys is very much like that in children, but is much more fatal; in fact, so large a proportion of inoculated monkeys die that the study of the affection clinically in them is difficult. No instances as yet have been reported in which one monkey has taken the disease from another, although long continued and intimate contact has been maintained.

The incubation period in monkeys is from five to forty-six days, with an average of eight or nine days.

IMMUNITY

A child or animal that has once had the disease becomes apparently immune and the blood of children and monkeys recovered from the disease has been found to render other monkeys refractory to subsequent inoculation, the specific antibodies persisting in the blood for three years in one case, but being absent in another case eleven years after the onset.[1] This fact, of course, suggests that a preventive serum may be hoped for, but as yet the serum treatment is wholly in an experimental stage, and not yet ready for use in cases of the human disease.

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[1] Netter and Levaditi: Comptes rend. Soc. de biol., 1910, lxviii, 855.

PERSONAL TRANSMISSION — DIRECT AND INDIRECT

In discussing the question of the transmission from patient to patient, the use of the technical and restricted term "contagious" will be avoided and the term "transmissible" will be employed.

The disease may be transmitted apparently in three ways: (1) By direct contact of a healthy child with a sick one; (2) by indirect contact by means of healthy persons passing from the sick to the well; and (3) in certain very rare instances a child has become ill shortly after occupying a house from which an affected family had moved.

Comparative Transmissibility.—The disease is, however, apparently less transmissible than other so-called contagious diseases with which we are more familiar.

In Minnesota a very careful investigation was conducted by Hill as to the relative transmissibility of infantile paralysis compared with that of scarlet fever, measles, etc., in the same territory. Of persons known to have been exposed to diphtheria, scarlet fever and infantile paralysis, the percentage contracting the disease was as follows: Scarlet fever, 22 per cent.; diphtheria, 17 per cent.; infantile paralysis, 6 per cent. Taking the instances of these same diseases, where one case existed in a family, the number of other cases occurring in the same family was as follows: Scarlet fever, 40 per cent.; typhoid fever, 30 per cent.; diphtheria, 29 per cent.; infantile paralysis, 17 per cent. The disease is thus apparently less transmissible than scarlet fever, typhoid fever or diphtheria.

The same evidences of mild transmissibility were shown in an investigation by Emerson, of an epidemic in the Deerfield Valley in Massachusetts in 1908, where a rural community offered excellent opportunities for study of contact. Furthermore, such instances as the following are difficult to explain by any theory of personal contact, direct or indirect:

In a sporting camp in a northern forest the 5-year old son of the proprietor had been in the camp since early spring. He had never left the camp during the summer. The camp was 5 miles from any other camp or house and 10 miles from the frontier town. There had been no other children in the camp during the summer and no illness of any kind in the guests or among animals. The few guests who were there came from the large cities, put on their hunting and fishing clothes and lived out of doors. In October the child developed a typical infantile paralysis, which still persists in one leg.

Evidence of transmission of the disease by personal contact from other epidemics is to be found in Wickman's Study, Shidler's report,[2] an epidemic observed by Frost,[3] and the Massachusetts studies.

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[2] Shidler: Pediatrics, 1910, xxii, 539.

[3] Frost: Public Health Bulletin 44.

Possible Factors Other Than Personal Transmission.—We come next to the consideration of the possibility of fruit, dust, insects, and animal paralysis as factors in the causation of infantile paralysis.

Fruit.—As to fruit, the high cost of living has undoubtedly led to a diminished consumption of meat, and presumably to an increased consumption of fruit. Traffic in fruit has increased steadily between 1900 and 1908, the increase being from one to two million tons a year, up to 1905, since which time there has been no such sharp increase. So far as these figures go, therefore, it would not seem that any very striking factor was to be found in this analysis. Common observation would, however, seem to show that in Massachusetts, at least, there are more fruit stores and apparently more fruit in use than was the case five years ago.

Dust.—In order to determine the rôle of dust in the etiology of infantile paralysis, the rainfall of the country was analyzed for two periods: first, the five years from 1900 to 1904; and second, the five-year period from 1905 to 1909, when we had the greater prevalence of the disease. The total rainfall during the last five years on the Atlantic seaboard has shown everywhere a diminution, reaching a high figure in New England. On the contrary, the regions in the middle west affected by the epidemic of infantile paralysis in 1909 showed an increased rainfall during the last five years, the rainfall being as much in excess of the normal as in New England it was deficient. In the middle Atlantic states, however, including New York, the rainfall in the two periods was practically the same. Excessive dryness in the last five-year period cannot, therefore, be put down as a condition pertaining to the affected regions, if one considers New England along with Nebraska and Minnesota. But we must remember that the germ is not injured by freezing or drying, and that the season of occurrence is certainly the season of greatest occurrence of dust. Moreover, a German observer found the disease in an unduly large proportion of shoemakers' children who were much in the shops where the dried dust was flying about, and the distribution of the disease along lines of travel suggests the possibility of such a mode of transmission.

Insects.—There are certain facts connected with the disease which suggest the possibility of its being transmitted by insects. This matter will be dealt with in speaking of the Massachusetts studies.

It has been shown experimentally by Flexner that if flies are allowed to feed on the cord of a monkey dying of the disease that they may carry the virus for forty-eight hours.[4]

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[4] Flexner, Simon and Clark, Paul F.: Jour. Am. Med. Assn., June 10, 1911, p. 1717.

Domestic Animals.—With regard to paralysis in the domestic animals, cases of paralysis strikingly suggestive are reported in horses, pigs, cats, dogs, rabbits, chickens, and other animals. A study of the distribution of animal paralysis in Massachusetts by means of letters addressed to veterinarians and animal inspectors showed, however, that in 1909 the distribution of cases of animal paralysis so reported did not in any way correspond to the distribution of the human disease for the same year, but much more extensive investigation along this line is necessary.

The conclusion must be that, in a consideration of etiology, infantile paralysis cannot be dismissed as a disease due only to transmission from patient to patient, but that these other factors must also be considered as possibly important.

Season of Occurrence.—In considering the etiology of the disease one is struck with the remarkably uniform seasonal occurrence which prevails in the north or in the tropics, in Europe or America. The disease begins to appear in the early summer, reaches its height generally in July, August or September, and diminishes through October, November and December, nearly to disappear in late winter and spring. In the southern hemisphere this behavior is reversed and the disease prevails most there in February and March, which is, of course, late summer and early fall in that locality.

Age.—The age of selection of the disease is between 2 and 3. Adult cases are comparatively uncommon, and occur chiefly in young adults. Dividing the ages into five-year periods, the following table was constructed by Frost:

Table 1.—Age Incidence in Five-Year Periods Expressed in Percentages

Age Years	N. Y. Commission (729 Cases)	Lovett (Mass.) (615 Cases)	Hill (Minn.) (325 Cases)
.....	Per cent. of Total	Per cent of Total	Per cent. of Total
Under 1	8.5	7.2	6.5
1 to 5	82.0	64.5	48.6
6 to 10	6.4	15.9	23.7
11 to 15	1.9	5.0	7.7
16 to 20	0.68	2.4	6.5
Over 20	0.40	5.0	7.0

General Incidence.—It affects all classes, rich and poor, in the cities and the country, in the tenements and in detached houses, on the top floor of houses, on the ground floor and in basements.

II. PATHOLOGY, SYMPTOMS, DIAGNOSIS, PROGNOSIS, PREVENTION AND TREATMENT

General Grouping of Symptoms and Types.—As a working hypothesis we may keep in mind the following as to symptoms and types of paralysis:

The infection enters the body by channels as yet unknown. In some instances this infective agent causes death from general paralysis due to extensive destruction of certain spinal and cerebral centers; in a second class of cases this agent causes some permanent loss of power in part or all of one or more limbs, the back, the abdomen, or in groups of muscles supplied by cranial nerves. In a third class, the same agent causes a very local yet probably permanent paralysis in one small muscle or small group of muscles, e. g., the extensor muscles of one little finger or certain muscles of the spine.

In a fourth class, weakness or transitory paralysis ending in recovery occurs as the result of the same infection. And lastly, in a fifth class, the infective agent causes fever, prostration and perhaps pain, but does not cause sufficient destruction to bring about any paralysis or weakness.

If we recognize this descending scale in the severity of the disease as depending probably either on the dose of the poison received or on the resistance of the individual, and recognize that the involvement of the spinal centers is perhaps after all incidental rather than essential, we may well believe that the disease is far more prevalent than is generally supposed, and especially in its abortive forms.

PATHOLOGIC ANATOMY AND HISTOLOGY

The characteristic lesions of the disease are found in the spinal cord and are most marked in the anterior horns of the gray matter of the cervical and lumbar enlargements.

In the gray matter in the early stages of the lesions are

1. Congestion of blood-vessels.

2. Edematous softening, sometimes accompanied by hemorrhage.

3. Infiltration with cells. (The cells diffusely infiltrate as well as aggregate together in foci and about the blood-vessels. They are of various kinds, but are chiefly lymphocytes and larger cells whose origin is not generally agreed on, and which are sometimes phagocytic.

4. Degeneration and diminution in the number of nerve-cells. The cytoplasm of the nerve-cell becomes hyaline and disappears leaving the nucleus naked and necrotic, and it also eventually disappears. The degenerated cell may be surrounded and invaded by the infiltrating cells. All of the nerve-cells in a given area do not always show degenerative changes, and more of them may be involved in one side of the cord than in the other. In the later stages of the disease, in extensively affected regions, nerve-cells and their processes are absent, the tissue is disintegrated and there is infiltration with phagocytic cells, plasma cells, proliferated glia cells, and connective tissue cells. Eventually, neuroglia with some connective tissue replaces the disorganized tissue and the part may appear atrophied to the naked eye.

In the white matter in the early stages of the disease, the lesions consist of congestion, edema and cellular infiltration of the adventitial lymph spaces of the blood-vessels and to a slight extent of the white matter as well. The infiltrating cells are chiefly lymphocyte-like cells. Small foci of these cells have been noted in the white matter. In some cases, acute degenerative changes have been observd in the anterior roots.

The pia mater also shows some infiltration, chiefly with lymphocytes, which is greatest in the anterior portions of the cord in the lumbar and sacral regions.

In the spinal ganglia there may be the same infiltration as in the white matter, without marked changes in the ganglion cells.

In the later stages of the disease there is degeneration and atrophy of nerve fiber tracts, anterior roots, motor nerves and muscles, depending in extent and location on the nerve-cells which have been destroyed.

In the medulla and pons similar lesions to those in the cord are found, but the degeneration of the ganglion cells is not so extensive as in the cord.

The brain as a rule shows comparatively slight lesions. Congestion of blood-vessels, small hemorrhages, cellular infiltration of the vessel sheaths and of the brain substance in foci have been observed in various situations. In old cases, foci of sclerosis have been observed.

In acute cases, the thoracic and abdominal organs show changes which may be observed in other acute infectious diseases. A hyperplasia of the lymph-adenoid tissue of the intestine, mesentery and spleen is commonly observed in addition to acute degeneration of the myocardium, liver and kidneys, and there may be bronchopneumonia.

There is nothing in the pathologic anatomy and histology of the disease which shows the mode of entrance of the infectious agent into the body nor whether it reaches the central nervous system by the blood or by the lymph-stream.

SYMPTOMATOLOGY OF INFANTILE PARALYSIS

It is impossible in the time at our disposal to give more than the most cursory description of the symptomatology of this disease. If we think of it as a poliomyelo-encephalitis with meningeal complications and appreciate the fact that the disease may affect any or all parts of the gray matter of the central nervous system, and in all possible combinations, it is easier to understand the innumerable manifestations of the disease and it is less likely to be overlooked and mistaken for other conditions. The best classification of the various manifestations of the disease is that of Wickman, which is as follows:

1. Ordinary spinal paralysis; anterior poliomyelitis.
2. Progressive paralysis, usually ascending, less often descending; Landry's paralysis.
3. Bulbar paralysis; polio-encephalitis of pons.

4. Acute encephalitis; giving spastic mono- or hemiplegia.
5. Ataxic type.
6. Meningitic type.
7. Polyneuritic; multiple neuritic type.
8. Abortive type.

Initial Symptoms.—It will be well, perhaps, before taking up the special clinical types of this disease to consider briefly its initial symptoms and the possibilities of making a diagnosis before the appearance of the paralysis. There is, in the vast majority of cases, nothing characteristic about the onset. The symptoms are, in general, those of an acute infection. In many instances, however, gastro-intestinal symptoms predominate, while in others those referable to the respiratory tract are the most marked. Sweating, marked nervous irritability and general hyperesthesia are present in many instances before the onset of the paralysis, but they are not at all constant. Their presence points strongly toward this disease but their absence does not count against it. It is safe to say, therefore, that at present there is nothing about the early symptoms to justify a positive diagnosis of infantile paralysis before the onset of the paralysis, although the appearance of the symptoms of an acute infection in a child, known to have been exposed to this disease or during an epidemic, especially if accompanied by sweating, nervous irritability and general hyperesthesia, are sufficient to justify a probable diagnosis.

A leukopenia has been found in animals during the late prodromal and early part of the acute stage. It is, however, not a constant symptom in man and is often replaced by a hyperleukocytosis. It is possible that there is a lymphocytosis in the early stages, but the evidence at present is not sufficient to show whether it is at all constant. It is possible that both the absolute and differential count of the leukocytes may prove useful in the early diagnosis of infantile paralysis. At present, however, they are of little or no assistance.

Experimentally, there is an increase in the number of cells in the cerebrospinal fluid during the prodromal stage, the polynuclear cells at this stage outnumbering the mononuclear. After the appearance of the paralysis, however, the mononuclear cells quickly exceed the polynuclear. A fibrin clot is also often formed during the prodromal or early part of the acute stage. The cerebrospinal fluid, in the only reported instance in which it has been examined in man during the preparalytic stage, was slightly opalescent, gave a marked protein reaction with Noguchi's test and showed an excess of polynuclear cells. The formula had begun to change to the lymphocytic, however, before the appearance of the paralysis. It seems safe to say, therefore, that in most instances a positive diagnosis of infantile paralysis can be made in the preparalytic stage by means of lumbar puncture, and that this is the only way in which a positive diagnosis can be made at this time. The value of this procedure is considerably limited, however, by the variability of the early symptoms and the consequent lack of anything to definitely suggest its use. In order to recognize the disease early, therefore, before the onset of the paralysis, it would be necessary to do a lumbar puncture on every sick child, which hardly seems a rational procedure.

Abortive Type.—What has been said as to the symptomatology and diagnosis of the preparalytic stage of infantile paralysis applies equally well to the abortive type (Type 8 under Wickham's classification), meaning by this term the type in which there is never any paralysis. There has been some doubt as to the existence of this type in the past, because there was no way of positively proving that the cases supposed to be of this type really were examples of this disease at all, the evidence being merely presumptive. Flexner and Clark and Frost have, however, recently demonstrated the presence of specific immune bodies in the blood of persons supposed to have had abortive attacks of infantile paralysis. The blood serum of these patients inactivated the virus of the disease, so that the infection of monkeys was impossible. There is no doubt, therefore, that abortive cases do occur. It is probable that they are as common as, if not more common than, those with paralysis. The importance of the recognition of these cases, if the present conception as to the rôle of "carriers" in the spread of the disease is correct, is obvious.

1. Ordinary Spinal Type.—It hardly seems necessary to take up in detail the symptomatology of this type, with which everyone is familiar. The paralysis reaches its maximum in from a few hours to three or four days, is followed by a stationary period of from one to four weeks, which is in turn followed by a period of improvement, lasting from six months to a year, the final paralysis always being less than the initial. It is impossible to prophesy in the acute stage how extensive the final paralysis will be. In general, however, the final paralysis varies directly with the initial. The final paralysis is always flaccid; its distribution usually monoplegic or hemiplegic. In most instances some of the muscles of the paralyzed extremity escape; not infrequently only one or two are involved. The reflexes are diminished or absent, sensation is only exceptionally impaired. Deformities develop as the result of contractures of the nonparalyzed muscles.

It is not very uncommon for other muscles than those of the extremities to be involved, while these escape. Such muscles are most often the erectors of the spine and the abdominal muscles. The involvement is, moreover, not infrequently unilateral. The extensor muscles of the neck, those of one side of the spine or of one side of the abdomen may, for example, be alone involved. The deformities resulting from the paralysis or paresis of these muscles are often misunderstood and attributed to other causes.

2. Progressive Type.—In this type the paralysis usually appears first in the legs, and gradually extends upward. In rare instances it appears first in the arms, extends downward and finally upward to the muscles supplied by the medulla. It is probable that the great majority of the cases that have in the past been described under the term of "Landry's paralysis" really were examples of this type of infantile paralysis. When the paralysis reaches the external muscles of respiration, as it very often does, death is practically inevitable and usually occurs on the third or fourth day. The diaphragm is also sometimes involved. Death occurs sooner, of course, when this happens. This form must not be confused with that in which death results from respiratory paralysis due to involvement of the centers of respiration in the medulla.

3. The Bulbar Type.—Cases of this type have in the past been usually designated as polio-encephalitis superior or inferior, according to which of the cranial nerve nuclei were involved. The nuclei may be affected singly or in all possible combinations. The symptoms depend, of course, on the nuclei involved. The facial and abducens nerves are perhaps the most often affected. There may be paralysis of deglutition and of the muscles of the larynx. When the vagus is involved there are disturbances of respiration and of the cardiac action. In such instances, the respiration is often of the Cheyne-Stokes type and the prognosis is practically hopeless. Involvement of one or more of the cranial nerve nuclei is not very uncommon in connection with the ordinary spinal type of infantile paralysis. When this happens the resulting picture is a combination of the two types.

4. Acute Encephalitic Type.—This type was described by Strümpell many years ago under the term, "acute encephalitis of children," but it has only recently been recognized as a variety of the disease under consideration. The symptoms resemble those of acute meningitis, the deep reflexes are, as a rule, exaggerated and the paralysis is spastic. The diagnosis is usually impossible without lumbar puncture. The prognosis as to life is better than it would appear and that as to recovery from the paralysis much better than in paralysis due to other cerebral diseases.

5. The Ataxic Type.—Ataxia is a prominent symptom in a certain number of cases. In a few, it is the only nervous symptom; in others, it is associated with paralysis of the cranial nerves and sometimes with a small amount of spinal paralysis. The ataxia is often distinctly of the cerebellar type.

6. The Meningitic Type.—Symptoms of meningeal irritation are not at all uncommon in the early stags of all types of infantile paralysis. These are so marked in many instances that they present the typical picture of meningitis. Headache, rigidity of the neck and back, vomiting, tonic and clonic spasms, strabismus, Kernig's sign, delirium, coma and other signs of meningeal irritation may be present in any and all combinations. In such cases the diagnosis on the symptomatology alone is impossible before the appearance of the flaccid paralysis. Even then it is open to doubt, because flaccid paralysis is not very uncommon in meningitis, especially if it is of the tuberculous type.

A positive diagnosis can only be made in most instances by lumbar puncture. The characteristics of the cerebrospinal fluid during the preparalytic stage have already been mentioned. During the acute stage it is clear, not infrequently under somewhat increased pressure, often forms a fibrin clot on standing and always contains an excess of protein and of cells. The cells are chiefly of the mononuclear type, most of them being lymphocytes. These characteristics are, however, the same as those found in tuberculous meningitis, the type of meningitis with which infantile paralysis is most likely to be confused. A positive diagnosis between them can only be made, therefore, by the examination of the cerebrospinal fluid for tubercle bacilli. The characteristics of the cerebrospinal fluid in meningococcal, influenzal and pneumococcal meningitis are so different from those in infantile paralysis that no confusion with these conditions is possible.

The Polyneuritic Type.—Pain is a prominent symptom in many instances. It is sometimes located in the joints, but is more often along nerve-trunks or indefinite in its distribution. It is usually most marked in the paralyzed parts. There is occasionally tenderness over the nerve-trunks. The pain and tenderness are sometimes marked enough to cause the paralysis to be entirely overlooked and a diagnosis of rheumatism or scurvy to be made.

The extremities are often held rigidly and all motion as vigorously resisted as possible, because of the pain on motion. This combination of rigidity and resistance is possible, of course, only when the muscles are partially paralyzed or when some of them are intact. The failure to appreciate the significance of this combination of flaccidity and spasticity not infrequently leads to errors in diagnosis during the acute stage.

PREVENTION

The question of the prevention of the disease is of great importance, and you are probably asked as frequently as we are in Massachusetts: "What shall I do to protect my children from the disease?" — a question which we must answer fairly with due regard to the interests of the patient, remembering, however, that advice too radical will increase the panic which is sure to appear in a locality where the disease is prevalent. It seems proper to advise people with children that, other things being equal, it is wise not to go for the summer to a locality where the disease is known to be prevalent. If, however, people find themselves in such a locality, the children and members of the family should keep away from other children who are in the acute stage of paralysis, and from children who are sick with other indefinite ailments.

In such localities it would seem wise to keep children away from children's entertainments, circuses and electric cars, and to prohibit playing with sick or paralyzed domestic animals.

Length of Quarantine.—We have at present no data as to how long the infectious period of the acute stage lasts, and any attempt to determine the length of quarantine must be mere guesswork.

With regard to the necessary length of quarantine, general consent has placed it at from two to four weeks. The recent experiments of Osgood and Lucas in this matter are, however, important inasmuch as they found an active virus in the nasopharyngeal mucous membrane of a paralyzed monkey, five and one-half months after the active stage of the disease had passed. The virus disappears from the nervous system in three or four weeks, or less, according to Flexner's experiments.

MORTALITY

The death-rate is about seven or eight per hundred, as the disease has existed in Massachusetts, but no foreign statistics show as low a figure as this, being from 10 to 22 per cent. In persons older than 10, the mortality-rate is higher than between 1 and 10, and under 1 year the disease seems more fatal.

The mortality table is interesting as showing the difference between the foreign and American death-rate.

TABLE 2.—COMPARISON OF FOREIGN AND AMERICAN DEATH-RATE

	Year	Cases	Death	Mortality Per cent.
	....	....	....	
Caverly, Vermont	1894	132	18	14.5
Wickman, Sweden	1905	868	145	16.7
Leegaard, Norway	1905	577	84	14.5
Zappert, Austria	1908	266	29	10.8
Lindner and Mally, Austria	1908	71	16	22.5
Furntrat, Steiermark	1908	433	57	13.1
Krause, Germany	1909	633	78	12.3
Muller, Germany	1909	100	16	16.0
Peiper, Germany	1909	51	6	11.7
Eichelberg, Germany	1909	34	7	20.6
Mass., U. S. A.	1907-1910	1,599	125	7.9

The mortality of cases in older children and in adults is higher than in other classes.

TABLE 3.—SHOWING HIGHER MORTALITY IN THE MORE ADVANCED AGES

	Age	Mortality, Per cent.
	....	
Wickman	12 to 32	27.6
Leegaard	15 to 30	25.8
Furntrat	Over 15	25.5
Lindner and Mally	Over 11	50.0
Mass., 1910	Over 10	20.0

PROGNOSIS

A few years ago it was supposed by most persons that practically all patients once paralyzed were to some extent paralyzed for life. But more careful study has shown us a better and more encouraging state of affairs. In the cases in Massachusetts, in 1909, a group of 150 occurring near Boston were studied in detail and it was reported that twenty-five, or 16.7 per cent., had wholly recovered inside of three months. This statement was not believed and the investigators were sent back to review their work. Each one of the children was stripped and the movements of ankle, knee, hip, shoulder, elbow, wrist and spine were examined. The statement can be definitely made, therefore, that, of this group, 16 per cent. had wholly recovered within three months.

The commonest type of final paralysis is an affection of one leg varying in degree from a slight limp in walking to a condition which requires the use of a brace; if both legs are involved, crutches are occasionally also required.

In short, a disability from infantile paralysis so great as to prevent an adult from earning his or her own living, occurs in a very small number of patients properly treated, but the ultimate condition of neglected cases is frequently distressing.

In connection with the question of treatment it is important to consider the reasons for this tendency to recovery, which are to be found in the pathology of the disease.

At the height of the disease there is an extensive perivascular infiltration of the blood-vessels of the cord, diminishing their lumen and inducing anemia and edema of the regions of the cord supplied by them. In addition to which there is also inflammatory edema of the nerve-tracts in the white matter and edema of the nerve-cells in addition to any destructive process which may be going on in neighboring cells. These changes, of course, cause loss of function in the parts affected, expressed as a temporary paralysis which passes away as the perivascular infiltration subsides. This apparently accounts for the improvement of paralysis in the early stage of the disease which exists in all non-fatal cases.

But the spontaneous improvement in the paralysis of the early history of the disease is no more important than improvement to be obtained by proper treatment in the chronic stage of the disease, after there is every reason to believe that the temporary perivascular infiltration has subsided, and the reason for this later improvement apparently rests on another pathologic basis. Assuming that the phenomena just described have ended, but that permanent destruction of certain motor centers in the spine has occurred, leaving a definite motor paralysis, the question arises, What reason is there to look for improvement in this? The answer apparently is as follows:

The spinal motor centers are grouped in cigar-shaped bundles whose length lies in the long axis of the spine. At each level of the spine are several of these bundles which overlap each other and communicate freely. Each bundle furnishes impulses to more than one muscle and each muscle receives impulses from more than one bundle. The blood-supply of the spine comes in horizontally and the lesions of this disease are most marked around the vessels. The distribution of the destructive process is therefore likely to be horizontal, while the distribution of the motor bundles is longitudinal. For this reason it is likely that if the destruction has not been too extensive, certain parts of the motor bundles will have escaped, leaving certain cells in some of them capable of function but which, in order to perform function, must acquire new connections and new groupings.

For this reason it will be seen, as will be maintained later, on the ground of practical experience, that muscle-training offers the best hope of the restoration of power to affected muscles in the chronic stage of the paralysis. It is an attempt to bring motor impulses from the brain down to the affected centers in the cord, there to establish new connections and new routes to the paralyzed muscles. The more impulses of this sort, however feeble they may be at first, to reach the affected muscles the better the chance of establishing finally routes which may serve for the transmission of impulses strong enough to secure efficient muscular contraction.

TREATMENT — ACUTE STAGE

In the matter of treatment much progress has been made in the last four years. In the acute stage meddlesome and useless treatment by stimulating drugs and counter-irritants has become largely discredited. Rest is very important, although cathartics and hexamethylenamin are of probable value, the latter drug being used with the object of setting free formaldehyd in the cerebrospinal fluid. Indeed, it has been shown experimentally that if hexamethylenamin is administered by mouth to monkeys, and if such animals are subsequently inoculated either subdurally or by the intracerebral route, paralysis is, in a certain proportion of cases, delayed or prevented. The value of the drug, therefore, in the prevention of infection would seem to be indicated, but there is as yet no experimental evidence to show that the drug is of much use after the disease has once begun.

In view of the pathologic condition, it is simply common sense to keep the patient recumbent and quiet and to avoid irritation of the muscles supplied by the affected nerve-centers. Massage and electricity should not, therefore, be used until there is reason to believe that subsidence of the inflammation has taken place. We may probably interpret the tenderness of the limbs as showing, while it lasts, the persistence of some degree of spinal or neural inflammation and until that has wholly disappeared we are not justified in the use of passive movements, massage or electricity.

Some men of large experience discourage all active treatment before the expiration of six weeks at least, but excellent results are frequently obtained by beginning treatment earlier on cases characterized by slight and transient tenderness. We should, however, discourage all active treatment until tenderness has wholly disappeared.

Another point of primary importance in early treatment is the prevention of contractures and deformities due to unopposed muscular action. Except in paralysis of the back and shoulder these contractures and deformities are always preventable, the contracture of the tendo Achillis, e. g., which is so frequent and so troublesome, being easily prevented by the use of splints supporting the foot at a right angle.

We read much concerning the relative merits of electricity and massage in the restoration of muscular power, but who shall pronounce as to the value of either in an affection in which paralysis varies so much in extent and severity and the recovery from which is so surprisingly different, irrespective of methods of treatment? Both methods have as an object the stimulation of muscular fibers and the maintenance of muscular nutrition, but both are inferior to muscular training in active treatment. This method of treatment is most useful in connection with massage or electricity and aims to cultivate the transmission of a voluntary motor impulse from the brain, down the cord to the paralyzed, weakened or stretched muscles. A flicker of motion, in an affected muscle, is often the forerunner of a return of some degree of power, and assistance by the hand in performing voluntary movements of the foot, for example. is often of great use.

Apparatus.—As to the use of apparatus, when a child in attempting to stand cannot, for example, hold the knee extended in weight-bearing, or when he stands in a position of deformity, for instance, with flat foot, apparatus should be applied to restore normal relations. Nothing but harm can result from sitting or going about with a curved spine, a hyperextended knee, or a foot rolled over on its inner or outer border. Stretching of muscles and ligaments and permanent bony deformities which are sure to result are worse than the use of braces, objectionable as the latter are.

Contractures which exist in neglected cases are not extremely resistant early in their history and must be removed before satisfactory mechanical treatment can be carried out. Most of them can be removed if stretched by means of bed traction or by the use of a series of correcting plaster bandages or by cutting. Operative treatment, except for the minor tenotomies, should not be undertaken for two years after the attack and preferably not then in children under 10.

Surgical Treatment.—Operation.—Tendon transplantation is a most useful measure and now that it has passed through its period of extravagant claims and unjustified condemnation, it may be said, in properly selected cases and with proper technic, to produce generally satisfactory and often brilliant results.

It consists in transplanting the distal end of a healthy muscle to the periosteal insertion of a paralyzed one, the foot or knee or arm being thus rebalanced. Since we have learned to prolong tendons by silk, the range and application of the operation has increased. We plan our operation, dissect and cut off our good muscle and if it is too short lengthen it at its distal end by heavy silk, we then insert it where we like, a new and sound tendon forming around the silk. In this way peroneals may replace tibials at the ankle or *vice versa,* hamstrings may be carried forward and inserted into the tibia to serve as knee extensors when the quadriceps is paralyzed and the trapezius may be substituted at the shoulder for a paralyzed deltoid.

Arthrodesis.—As a means of stiffening and making stable useless joints, arthrodesis has been found a useful measure. This operation consists in opening such joints and removing enough cartilage to secure ankylosis, and is applicable to the hip, ankle, elbow, and shoulder in children over 12, and to the knee in adults but not to the knee in growing children.

Silk Ligaments.—For the correction of foot drop in paralyzed legs we have made use more and more of anterior silk ligaments, the idea being to prevent plantar flexion of the foot but still to allow dorsal flexion. Heavy strands of silk are sewed into the anterior surface of the tibia, carried down under the annular ligament of the ankle and sewed into the dorsal surface of one of the tarsal bones. This operation is distinctly preferable to arthrodesis.

Nerve transplantation has not yet emerged from its experimental stage.

Finally, one of the most important things that orthopedic surgeons have learned of late years is that the hope for improvement in these cases through efficient and suitable treatment need not be given up in six months or one year or ten years, but that the possibility of improvement seems to persist almost indefinitely.

III. INFANTILE PARALYSIS AS OBSERVED IN MASSACHUSETTS, 1907-1910

The investigation of infantile paralysis in the state of Massachusetts by the State Board of Health for the four years, 1907 to 1910, inclusive, shows that during that period 2,138 cases of the disease were reported to the office of the State Board of Health. These cases were distributed by years as follows:

1907	234
1908	136
1909	923
1910	845

It is apparent from these figures that the disease in Massachusetts has, in a general way, during the period mentioned, increased in frequency, and it has been shown that a larger number of towns were infected each year.

Two-Year Periodicity.—There is, moreover, in these figures a suggestion of what may be an important phenomenon, and that is the appearance of a two-year periodicity for this disease. This phenomenon is noticeable in the distribution in general. In 1905 occurred the great Scandinavian epidemic. In 1906 there were no important epidemics. In 1907 occurred the New York epidemic. In 1908 there were only a few small epidemics and none of importance reported in Europe. In 1909 occurred the Massachusetts, Minnesota and Nebraska epidemics, two large and one small German epidemics, a large outbreak in Austria and the epidemic in Cuba. In 1910 from Europe no large epidemics were reported so far as we have been able to learn. The occurrence of the disease in this country in 1910 has already been dealt with.

This two-year periodicity has been noted a number of times in our investigation; for instance, in 1907 the western part of the state was quite sharply affected with infantile paralysis, whereas in 1908 the disease was almost non-existent in that same region. Again in 1909 the disease cropped up, but in 1910 hardly any evidence of infantile paralysis was noted in that neighborhood. In 1908, furthermore, in the Turners Falls district, etc., a very marked epidemic occurred, involving sixty-nine cases in a quite sharply circumscribed locality. In 1909 but one case occurred in this whole region. So that one can prophesy, to a certain extent, at least, that a limited locality, severely affected during one year, will probably enjoy partial immunity in the succeeding year. On the other hand, many localities having the disease to a moderate extent seem to go on from year to year at about the same rate.

Relative Prevalence in Smaller Cities and Towns.—Infantile paralysis is a disease affecting by preference the smaller cities and towns. This statement rests on the observation of 2,138 cases in Massachusetts, which have been analyzed in this regard.

The incidence per 1,000 of the population was recorded for every affected city and town in the state for four years. For each year the cities and towns were then arranged in the order of greatest incidence and then the first twenty-five on the list were contrasted with the last twenty-five for each year.

The average population for the first twenty-five was then reckoned for the four years and proved to be 5,205. The average population of the last twenty-five on the list, those where the incidence was least, was 52,674. A further study of the table shows that some such proportion as this existed in every one of the four years. That is to say, cities and towns where the disease was relatively least frequent were ten times as large on the average as those where it was most frequent. Furthermore, as a control, we tabulated the cases of scarlet fever reported in the state for the year 1910 in the same way. In the twenty-five cities and towns in which scarlet fever was most prevalent the average population was 6,446, and in the twenty-five where it was least prevalent per 1,000 of the population the average population was 7,633, practically the same, showing that scarlet fever showed no such predilection for the smaller cities and towns (Table 4).

TABLE 4.—COMPARATIVE PREVALENCE OF INFANTILE PARALYSIS AND SCARLET FEVER WITH REFERENCE TO POPULATION OF CITIES

Disease	Twenty-five Cities Where Disease was *Most* Prevalent	Twenty-five Cities Where Disease was *Least* Prevalent
Acute epidemic poliomyelitis	5,205	52,674
Scarlet fever	6,446	7,633

In seeking to analyze some of the conditions which were constant in the smaller cities and towns which did not prevail in the larger, the number of domestic animals in each city and town was looked into and the analysis contributes the information that the number of such animals is relatively very much greater in the smaller cities and towns than in the larger. Such a fact may have no significance whatever, or it may in the future prove of importance (Table 5).

TABLE 5.—PREVALENCE OF INFANTILE PARALYSIS WITH REFERENCE TO THE NUMBER OF ANIMALS IN CITIES AND TOWNS

Total Number of Animals Assessed in Twenty-five Cities and Towns where the Disease was *Least* Prevalent, i. e., in the larger Cities and Towns.		Total Number of Animals Assessed in the Twenty-five Cities and Towns where the Disease was *Most* Prevalent, i. e. in the smaller Cities and Towns.	
Total population	.943,614	Total population	142,639
Total number of cows	11,160	Total number of cows	12,801
1 cow to 84.5 inhabitants.		1 cow to 11 inhabitants.	
Total number of horses	29,519	Total number of horses	10,352
1 horse to 32 inhabitants.		1 horse to 14 inhabitants.	
Total number of swine	3,288	Total number of swine	2,374
1 swine to 287 inhabitants.		1 swine to 60.5 inhabitants.	
Total number of fowls	41,887	Total number of fowls	79,797
1 fowl to 22.5 inhabitants.		1 fowl to 1.75 inhabitants.	
Total number of dogs	23,854	Total number of dogs	5,865
1 dog to 39.5 inhabitants.		1 dog to 24.3 inhabitants.	

Of course, this is only one of many conditions which are different in the two classes but the persistence year after year of this greater prevalence of the disease in the smaller cities and towns must mean something with regard to the etiology of the disease if we were only able to interpret it.

Seasonal Occurrence.—The occurrence of the disease by months shows that the maximum incidence of infantile paralysis occurs between June and November. In 1907 the largest number of cases occurred in September. In 1908 July and August had equal numbers; 1909 had the largest number in August, and 1910 in July. There seems thus to be in Massachusetts a distinct tendency of the maximum incidence to recede in point of time, a phenomenon which should it occur in 1911, might be worthy of serious investigation (see Charts 5, 6, 7, 8 and 9).

Age.—The combined experience of three years, 1908 to 1910, shows that 6.13 per cent. of the cases occurred before the end of the first year; 66.94 per cent. before the end of the fifth year, and 83.1 per cent. before the end of the tenth year. Moreover, the Massachusetts figures give the impression that the disease is more frequent in adults than has been commonly supposed (Table 6).

TABLE 6.—OCCURRENCE BY AGE PERIODS (1908-1910)

Age, Years	Cases	Per cent.
Birth to 12 mos., inc.	55	6.13
1	119	13.26
2	155	17.35
3	125	13.93
4	92	10.25
5	54	6.02
	600	65.94
6 to 10, inc.	145	16.16
	745	83.10
11 to 20, inc.	83	9.25
	828	92.3
21 to 30, inc.	39	4.34
31 to 72, inc.	17	1.89
Not stated	13	.....
	897	.....

Sex.—As far as sex is concerned, the relative incidence is expressed by the figures of 56 per cent. for males and 44 per cent. for females, as reported for the four years, 1907 to 1910 (Table 7).

TABLE 7.—SEX (1907-1910)

		Per cent.
Males	906	56.66
Females	689	43.08
Not stated	4	0.25
Total	1,599	.....

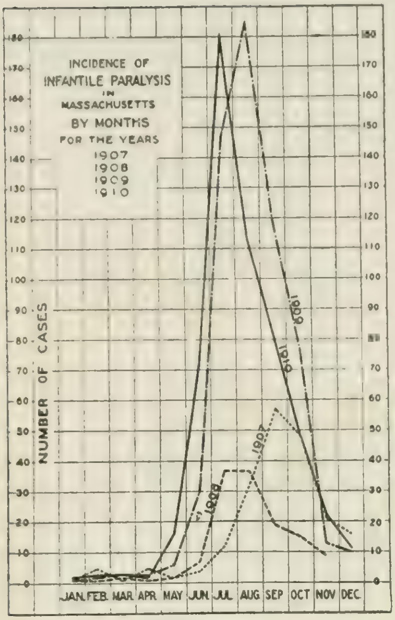

Chart 5.

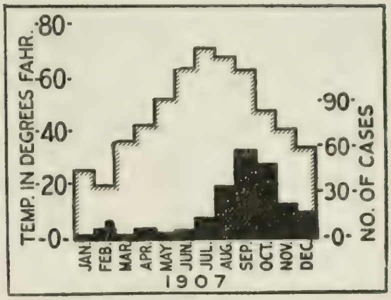

Chart 6

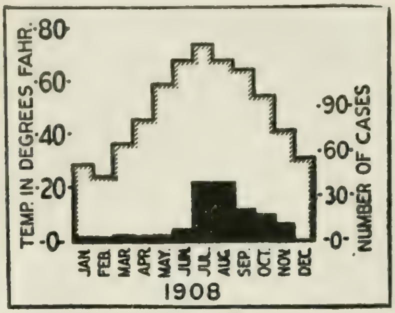

Chart 7

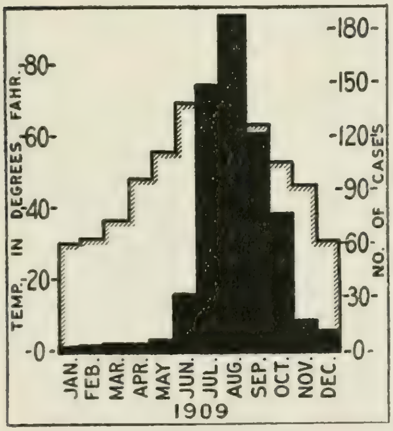

Chart 8

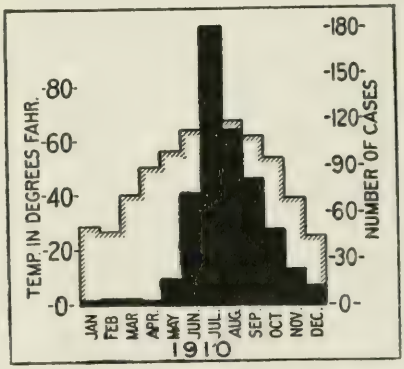

Chart 9

Chart 6.—Incidence of cases in 1907 by months shown in solid black; mean temperature in white.

Chart 7.—Incidence of cases in 1908 by months in solid black; mean temperature in white.

Chart 8.—Incidence of cases in 1909 by months in solid black; mean temperature in white.

Chart 9.—Incidence of cases in 1910 in solid black; mean temperature in white.

Mortality.—The mortality under 1 year is high, being for 1909-10 12.19 per cent. Between 1 and 10 years the fatality seems to drop. being 6.24 per cent., but after ten years the mortality again rises and reaches 14.81 per cent. The average mortality is 7.9 per cent. (Table 8).

TABLE 8.—MORTALITY BY AGE (1909-1910)

Age, Years	Cases	Deaths	Mortality, Per cent.
	....	.....	
Under 1	82	10	12.19
1 to 10	945	59	6.24
Over 10	189	28	14.81
Totals	1,216	97	.....
Average mortality			7.9

Environment of Patients.—As regards the character of the house, practically an equal number of cases occurred in detached houses, in tenements or in apartments. Furthermore, there seemed to be no marked predilection of the disease for any special floor of the house. The house was said to be dry in 72 per cent., damp in 27 per cent., and medium in 1 per cent. No apparent relation to moisture can, therefore, be made out. The sanitary conditions were either excellent, good or fair in 85.6 per cent. cases, and bad in only 11.5 per cent. The age of the house was not remarkable, 41.14 per cent. of patients living in new houses; that is to say, within the first and tenth year of its existence; whereas 58.85 per cent. lived in houses more than ten years old.

It has seemed at times as if the disease preferred river beds, but this factor in the occurrence of the disease must rest on other basis than mere propinquity, because, although thirty-three patients are said to have lived near a river or near water, 317 lived more than one-eighth of a mile from any stream, pond, or beach, so that it seems probable that any marked occurrence of the disease along the water courses is due to other factors than a neighborhood of water, the determining influence being in all probability increased personal contact due to the fact that all highroads, electric railways and railroads are very apt to follow river valleys, and cities and towns are, therefore, more likely also to be situated along such water courses.

In the same way, no especial relation could be found between the occurrence of infantile paralysis and nearness to railroads. The experience of Wickman, as shown by his maps, certainly seemed to show a distinct preference of the disease for localities near railroads, but in Massachusetts we have not been able to observe any etiologic connection between the two. In 1909-10, 30.56 per cent. of the cases occurred within one-eighth of a mile of the tracks, while 69.42 per cent. were more than one-fourth of a mile away.

A study of sewage condition shows that the disease occurs under all conditions of sewage disposal and as regards water supplies from metropolitan and city systems, as well as from wells and springs (Tables 9, 10, 11, 12, 13, 14, 15, 16 and 17).

TABLE 9.—CHARACTER OF HOUSE (1907-1909)

		Per cent.
Detached	220	49.54
Tenements	224	50.45
Total	444	.....

TABLE 10.—FLOOR OF HOUSE INHABITED BY FAMILY (1907 AND 1909)

		Per cent.
The whole house	75	21.06
The first floor	139	39.04
First floor and basement	3	.84
Second floor	101	28.37
Third floor	32	8.98
Upper stories	6	1.68
Total	356	.....

TABLE 11.—LOCATION OF HOUSE (1907-1910)

		Per cent.
Dry	459	71.38
Damp	177	27.52
Medium	7	1.08
Total	643	.....

TABLE 12.—SANITARY CONDITION (1907-1910)

		Per cent.
Excellent	123	18.83
Good	271	41.50
Fair	165	25.25
Bad	74	11.33
Not stated	20	3.06
Total	653	.....

TABLE 13.—AGE OF HOUSE (1909-1910)

		Per cent.
New House (1-10 yrs.)	144	41.14
Old House (over 10 yrs.)	206	58.85
Total	350	.....

TABLE 14.—NEARNESS OF HOUSE TO WATER (STREAM, POND OR BEACH)
(1909-1910)

		Per cent.
On river	33	9.42
Within ⅛ mile	66	18.85
Within ¼ mile	89	25.42
Within ½ mile	78	22.28
Within 1 mile	84	24.00
Total	350	.....

Table 15.—Nearness of House to Railroad (1909-1910)

		Per cent.
On railroad	57	16.28
Within ⅛ mile	50	14.28
Within ¼ mile	44	12.57
Within ½ mile	114	32.57
Within 1 mile	85	24.28
Total	350	.....

Table 16.—Character of Sewage Disposal (1908-1910)

		Per cent.
Sewage (Met.)	110	26.25
Sewage (City, etc.)	211	50.35
Cesspool	23	5.48
Vault	60	14.31
Privy	15	3.57
Total	419	.....

Table 17.—Character of Water-Supply (1908-1910)

		Per cent.
Metropolitan	120	27.98
Town	62	14.45
City	172	40.09
Well	17	3.96
Spring	58	13.51
Total	429	.....

Rainfall.—The deficiency in rainfall during the last eight years has been, of course, very marked, and this factor may be of importance in the spread of the disease. It certainly has to be taken very seriously into consideration if we accept the suggestion of Hill of Minnesota that dust, especially dust infected with horse manure, may be responsible for the transference of this disease. The deficiency of rainfall in Massachusetts has varied since 1904, when it was 1.35 inches, to 9.42 inches in 1910. With the deficiency of rainfall during each year of this period has occurred a sort of cumulative effect, which makes this deficiency relatively more important each year. A study of the deficiency of rainfall shows that the largest number of cases have not occurred in the driest years in Massachusetts (Table 18 and Charts 10, 11, 12, 13).

Table 18.—Deficiency Rainfall (1904-1910)

Year	Cases in State	Actual	Normal	Deficiency
....		......	......	....
1904	...	43.81	45.16	— 1.35
1905	...	37.60	.....	— 7.56
1906	...	43.21	.....	— 1.95
1907	234	44.49	.....	— 0.67
1908	136	37.61	.....	— 7.55
1909	923	42.10	.....	— 3.06
1910	845	35.50	.....	— 9.42
				—31.56

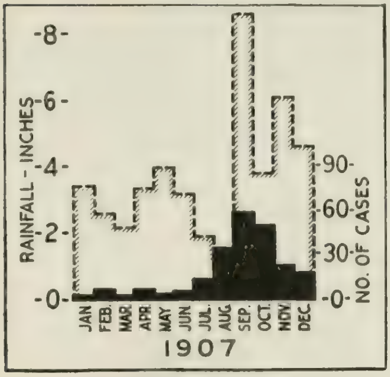

Chart 10

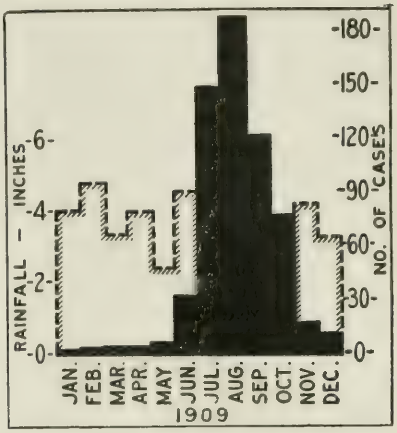

Chart 12

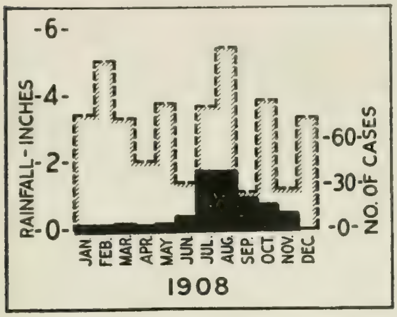

Chart 11

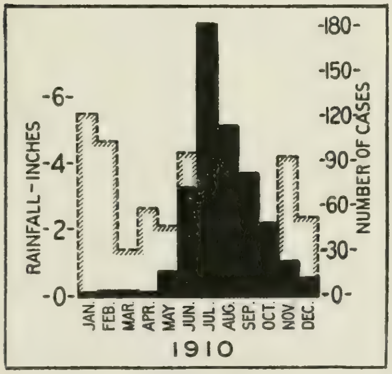

Chart 13

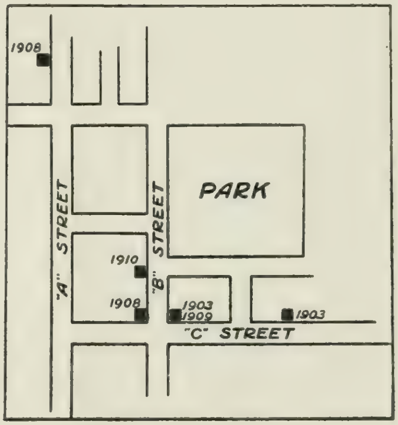

Chart 14

Chart 10.—Incidence of cases and rainfall by months in 1907. The former shown in solid black.

Chart 11.—Incidence of cases and rainfall in 1908. The former shown in solid black.

Chart 12.—Monthly incidence of cases and rainfall in 1909. The former in solid black.

Chart 13.—Monthly incidence of cases and rainfall in 1910. The former in solid black.

Chart 14.—Map showing endemic focus of infantile paralysis in a city of 119,000 inhabitants; cases occurring in the years 1903, 1908, 1909 and 1910.

Dust.—A study of the amount of dust in affected localities shows a report of a moderate amount in more than half of the cases while in 36 per cent. of the total number much dust or an excessive amount was reported. The matter is not, however, one capable of measurement or exact determination and the table cannot be regarded as important (Table 19).

TABLE 19.—RELATION TO DUST (1909-1910)

		Per cent.
No dust	0	.....
Very little dust	29	8.28
Moderate amount of dust	195	55.71
Much dust	118	33.71
Excessive amount of dust	8	2.28
Total	350	.....

Insects, Etc.—The possible transfer of the disease by vermin, insects, rodents, etc., was investigated, but the figures are not at all conclusive, and very little knowledge of value is likely to come in this department of the work, until individual infected localities are investigated by persons expert in the study of entomology, a line of investigation of the greatest importance (Table 20).

TABLE 20.—PRESENCE OF VERMIN, INSECTS, RODENTS, ETC. (1909-1910)*

		Per cent.
Flies	298	90.85
Mosquitoes	142	43.29
Mice (house)	123	37.5
Ants	97	29.57
Rats	77	23.47
Bedbugs	70	21.34
Roaches	64	19.51
Spiders	54	16.46
Mice (field)	24	7.31
Biting flies	10	3.04
Fleas	4	1.21
Grubs and Caterpillar	3	.91
Bees	2	.609
Sand fleas	1	.304
Snakes	1	.304
Crickets	1	.304
Squirrel	1	.304
Leeches	1	.304
Brown tail moths	1	.304
Moles	1	.304
Total	328 families	

*Report 1907 and 1908 only for flies and mosquitoes.

Domestic Animals.—The rôle played by domestic animals in the transfer of the disease is one of great possible interest, but as yet the interrelation of the paralyses of man with those of animals has not been sufficiently marked to justify any definite conclusion. Many cases of paralysis in animals have been reported, but the instances in which paralysis in human beings has been coincident with such animal paralysis have been rare (Table 21).

TABLE 21.—DATA AS TO DOMESTIC ANIMALS (1909-1910)

		Per cent.
No animals of any kind in	131	39.93
Animals in	197	60.06
125 animals had sickness, paralysis or death in	70	21.34
Total	328 families	

Transmissibility.—The degree of contagiousness of infantile paralysis is a question of great theoretic and practical importance. It is one which at the present time it is practically impossible to analyze exactly because, associated with the paralytic cases of this disease, occur an unknown number of so-called abortive cases which may be of the greatest importance in transferring to others paralytic types of the affection. Furthermore, these unknown abortive cases become immune to subsequent infection, and if included in any study of comparative contagiousness, will go far, undoubtedly, to vitiate any conclusions drawn. Our figures show that in 350 cases carefully studied, there was direct contact with an acute case in 13 per cent.; direct contact with possible abortive cases in 1.42 per cent.; with chronic cases in 4.28 per cent.; and that there was, undoubtedly, indirect contact with an acute case through a third person in 4 per cent. of the cases (Tables 22 and 23. See Chart 14 for an endemic focus in a city of 119,000 inhabitants).

TABLE 22.—INSTANCES OF CONTAGIOUSNESS (1909-1910)

Certain direct contact:		Per cent.
With acute case	46	13.14
With possible abortive case	5	1.42
With chronic case	15	4.28
With both acute and chronic cases	2	.57
Certain indirect contact with acute case by third person	14	4.00
Number of cases investigated	350	.....

TABLE 23.—FAMILIES WITH MORE THAN ONE CASE (REASON FOR SUSPECTING CONTAGION) 1908-1910

		Per cent.
One case	357	92.24
Two cases	27	6.97
Three cases	3	.77
Total	387	.....

Institution Cases.—Forty-four institutions for children in Massachusetts were written to in 1910, in order to ascertain whether or not any cases of acute epidemic poliomyelitis had originated within those institutions during the year. One institution, containing 360 children, in

Fall River, reported a single case, a boy, 4 years old. No secondary cases occurred in this institution (Table 24).

TABLE 24.—INSTITUTION CASES

	Cases	Incidence per 1,000
	....	
44 institutions with 3,600 children under 15 years of age	1	.277
Mass., with a population of 851,092 children under 15 years (Census of 1905) showed in 1910 cases of acute epidemic poliomyelitis under 15 years	532	.625

Children in institutions therefore would seem to be, in some measure and in some way as yet unexplained, protected from this disease. Their opportunities for contact with the outside world are obviously much curtailed in comparison with those of the ordinary child, and therein lies very probably the reason for their immunity.

Swimming, Etc.—Just prior to the disease, there was a history of swimming, wading, or paddling, in water more or less contaminated, in 25 per cent. of the cases just before attack (Table 25).

TABLE 25.—SWIMMING, WADING OR PADDLING (1908-1910)*

		Per cent.
Swimming, wading or paddling	105	25.05
No such history	314	74.94
Total	419	.....

*Water contaminated more or less in every instance.

Accidents.—In the same way, 34 per cent. of 457 cases gave a history of accidents, over-exertion or falls. With regard to the swimming, etc., the percentage would seem no higher than one would expect in any group of children at this season, living near the water. But the percentage of thirty-four accidents, falls and over-exertion just before the attack would seem perhaps unduly high (Table 26).

TABLE 26.—ACCIDENT, OVER-EXERTION OR FALL PRECEDING ATTACK (1907-1910)

		Per cent.
Accident	41	8.97
Over-exertion	47	10.28
Fall	67	14.66
No such history	302	66.08
Total	457	.....

Other Diseases.—A study of the disease prevalent in affected towns coincident with infantile paralysis showed nothing of importance. A further study of recent antecedent illnesses in the patient showed merely a number of minor ailments of no especial significance (Table 27).

TABLE 27.—DISEASES PREVALENT IN TOWN AT TIME OF OCCURRENCE OF INFANTILE PARALYSIS (1909-1910)

	Cases	Per cent.
Not known	159	46.49
Infantile paralysis	120	35.08
Whooping cough	12	3.508
Measles	11	3.21
Gastro-enteritis	8	2.33
Diarrhea	6	1.75
Influenza	6	1.75
Tonsillitis	4	1.16
"Rheumatic fever"	4	1.16
Scarlet fever	3	.87
Mumps	2	.58
Malaria	2	.58
Pneumonia	1	.29
Coryza	1	.29
Chicken pox	1	.29
Typhoid	1	.29
Diphtheria	1	.29
Total	342	.....

Diet.—The relation of diet to infantile paralysis is possibly of importance, but as yet no definite relation between the disease and certain kinds of food has ever been made out. Although evidently unusual, the disease does occur in breast-fed babies, four cases of the kind having been recorded in our returns of the last two years (Table 28).

TABLE 28.—DIET (1909-1910)

		Per cent.
General	283	80.85
(a) Raw cow's milk	308	88.00
(b) Condensed milk	15	4.28
(c) Breast milk and other food	19	5.42
(d) Breast milk alone	4	1.14
Fish	265	75.71
Fruit	288	82.28
Berries	197	56.28
Meat	275	78.57
Canned goods; (a) fruits; (b) vegetables; (c) fish	202	57.71
Cereals	140	40.00
Bread and butter	23	6.57
Vegetables	275	78.57
Stews and soups	11	3.14
Eggs	186	53.14
Tea, coffee, cocoa	6	1.71
Malted milk	2	.57
Ice cream	83	23.71
Predigested and beef juices	4	1.14
Candy	27	7.71
Bananas	6	1.71
For cases numbering	350	.....

Symptoms.—Digestive disturbances are common before, during and after the attack. Diarrhea is less frequent, comparatively, than constipation (Table 29).

TABLE 29.—DETAILS OF DIGESTIVE DISTURBANCE (1909-1910)

		Per cent.
PRECEDING ATTACK		
Nausea and vomiting	120	34.28
Constipation	109	31.14
Colic	5	1.42
Diarrhea	39	11.14
Indigestion or stomach upset	4	1.14
Mucus in stools	2	.57
ACCOMPANYING ATTACK		
Nausea and vomiting	140	40.00
Constipation	149	42.57
Colic	15	4.28
Diarrhea	56	16.00
Indigestion (indefinite)	3	.85
Mucus in stools	1	.28
FOLLOWING ATTACK		
Nausea and vomiting	5	1.42
Constipation	122	34.85
Colic	2	.57
Diarrhea	18	5.14
Mucus in stools	2	.57
Data for cases numbering	350	.....

The analysis of the general symptoms of the acute attack in 720 cases show fever present in 88 per cent., brain symptoms in 37 per cent., and retraction of the head in 34 per cent. Sore throat was only recorded as present in 9 per cent. (Table 30).

TABLE 30.—GENERAL FEATURES OF ACUTE ATTACK (1907-1910)

		Per cent.
Fever	636	88.33
Pain and tenderness	528	73.33
Brain symptoms	266	36.94
Retraction	248	34.44
Sore throat	65	9.02
For cases numbering	720	.....

Appearance of Paralysis.—The appearance of paralysis in relation to the attack was studied in 589 cases. In 16 per cent. paralysis occurred on the day of the attack; in 16 per cent., one day after the attack; in 17 per cent., two days after the attack and in 16 per cent., three days after the attack. That is to say, in 65 per cent., within three days after the attack. In two cases it was recorded as coming before the attack and in twenty-three cases (4 per cent.) between one and two weeks after the onset (Table 31).

Pain and Tenderness.—The great importance of pain and tenderness as a symptom is not sufficiently recognized; 1,198 cases were analyzed in this regard and in 70.5 per cent. these symptoms were present. The disappearance of pain and tenderness in an analysis of 604 cases, in which the time was recorded, occurred in 30 per cent. within one week.

in 15 per cent. in from one to two weeks, and in 13 per cent. in from two to four weeks. In five cases it was recorded as lasting two to three months and in three cases as lasting several months (Tables 32 and 33).

TABLE 31.—APPEARANCE OF PARALYSIS IN DAYS AND WEEKS AFTER ONSET OF FEVER (1907-1910)

		Per cent.
Preceding attack	2	.33
Same day	95	16.12
One day	93	15.78
Two days	103	17.49
Three days	98	16.63
Four days	58	9.84
Five days	22	3.73
Six days	51	8.65
Seven days	18	3.05
Eight days	6	1.01
Nine days	2	.33
Ten days	4	.67
Eleven days	3	.509
Twelve days	5	.84
Thirteen days	1	.169
Fourteen days	4	.67
Not known (fatal)	1	.169
2 to 3 weeks	6	1.01
3 to 4 weeks	1	.169
4 to 5 weeks	1	.169
8 weeks	1	.169
Two days previous	1	.169
Not stated	13	2.207
Total	589	.....

TABLE 32.—PAIN AND TENDERNESS (1907-1910)

		Per cent.
No pain	178	14.85
Pain	845	70.53
Not stated	175	14.6
Total	1,198	.....

TABLE 33.—DISAPPEARANCE OF PAIN AND TENDERNESS (1909-1910)

		Per cent.
1 day or less	11	1.82
2 days	22	3.64
3 days	29	4.801
4 days	15	2.48
5 days	14	2.31
6 days	3	.496
A few days	28	4.63
1 week	59	9.76
1-2 weeks	91	15.06
2-3 weeks	46	7.61
3-4 weeks	33	5.46
4-5 weeks	1	.16
6-7 weeks	1	.16
1-2 months	28	4.63
2-3 months	5	.82
Several months	3	.496
Until death	39	6.45
Present when report was made.	175	29.13
Total	604	.....

Distribution of Paralysis.—The distribution of paralysis was studied in 1,158 cases. The most common location was in one leg, occurring in 28 per cent.; both legs came next in frequency with 24 per cent.; one or both arms in 9 per cent.; and where one arm and leg were affected, a hemiplegic distribution was more common than a crossed paralysis, the relative percentages being 10 per cent. and 3 per cent. Special attention should be called to the frequent occurrence of paralysis of the back, abdomen, neck and face, which are much more frequent than is supposed and too often overlooked (Table 34).

TABLE 34.—DISTRIBUTION OF PARALYSIS (1907-1910)

		Per cent.
One leg only	324	27.97
Both legs only	272	23.48
Back	154	13.29
Both arms and both legs	129	11.13
One arm and leg, same side	110	9.49
One arm only	84	7.25
Both legs and one arm	75	6.47
Face	74	6.38
Abdomen	67	5.78
One arm and leg, opposite sides	33	2.84
Respiration	31	2.67
Both arms only	23	1.98
Neck	11	.94
Both arms and one leg	10	.86
Deglutition	7	.604
Neck and back	6	.51
Ataxia (transitory)	5	.43
General	3	.25
Intercostal	1	.086
Both arms, back, chest and throat	1	.086
For cases numbering	1,158	.....

Prognosis.—In order to throw additional light on the question of prognosis, Dr. B. E. Wood of Boston was requested by the Board to investigate the present condition of all patients reported to the Board as paralyzed in the year 1907. This inquiry was made with especial reference to the number of recoveries occurring in the four years which had elapsed. Letters were sent to all physicians who had reported cases in 1907, asking whether or not such patients had recovered, and when recovery was reported, such cases were seen unless they had disappeared or moved, and if such was the case all available information was obtained about the patients.

Of 234 cases, twenty-two could not be investigated, eleven had died in the acute stage of the disease; eight others had died subsequently of other diseases. Although two of them are said to have recovered from the paralysis, no trace could be found of three cases. In 212 cases, therefore, the termination is known, and fifty-seven of these (27 per cent.) are reported as having recovered.

On investigation it was found that there were three classes of recovery: (1) Complete recovery without atrophy, (2) recovery with complete function but with some atrophy, (3) recovery with some hypertrophy of the affected limb. The table shows the proportion of each of these.

TABLE 35.—CONDITION OF PATIENTS AFTER RECOVERY

		Per cent.
Complete recovery without atrophy	16	28.1
Functional recovery with atrophy	21	36.8
Recovery with some hypertrophy	3	5.3
Recovery, presence or absence of atrophy unknown	17	29.8

When atrophy was present, the maximum amount noted was as follows:

TABLE 36.—REMAINING ATROPHY AFTER RECOVERY

Calf	1¾ inches
Thigh	1¼ inches
Arm	½ inch
Forearm	¾ inch

In most cases the atrophy was much less than this, a difference of one-eighth inch being counted as atrophy, but in all such cases function of every muscle was perfect. The amounts of hypertrophy recorded were in two instances one-fourth inch and in one, three-eighths inch, all of the calf.

In these cases the severity of the attack was classed as:

TABLE 37.—SEVERITY OF THE ATTACK

		Per cent.
Severe	14	24.5
Moderate	9	15.9
Mild	28	49.1
Not noted	6	....
	57	....

The distribution of the paralysis in the fifty-seven recovered cases was as follows:

TABLE 38.—DISTRIBUTION OF THE PARALYSIS

One lower extremity	12
Both lower extremities	9
One upper extremity	6
Both upper extremities	2
One lower and one upper extremity	10
Three extremities	7
Four extremities	5
Face alone	1
General	1
Not given	4

In addition to this distribution, paralysis of the face also existed in four, of the back in five, of the face and back in one, and of the abdominal muscles in one.

The time of recovery in the fifty-seven cases was as follows:

TABLE 39.—TIME OF RECOVERY

1 week or less	2
1 week to 1 month	8
1-2 months	8
2-3 months	5
3-6 months	10
6-12 months	9
1-2 years	5
2-3 years	5
No data	5

CONCLUSIONS AS TO PROGNOSIS

The following conclusions seem justified as regards prognosis:

1. Complete recovery or functional recovery occurs in something over 25 per cent. of patients examined at the end of four years.

2. Atrophy may exist without impairment of function.

3. In about half of the recovered patients the onset was mild.

4. The distribution of the paralysis in such cases was not essentially different from that of cases which do not recover.

5. The period of recovery in many instances occupied months, and in several cases from one to two years.

234 Marlboro Street—145 State House.

PYLORIC STENOSIS IN OLDER CHILDREN, WITH REPORT OF A CASE OF PYLORIC SPASM ENDING FATALLY

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It is not my intention to study in this paper the condition spoken of as congenital pyloric stenosis in infants, but to consider stenosis of the pylorus in children who have passed the period of infancy. The study of the condition in older children must, however, embrace those patients in whom the condition has persisted from infancy into later childhood, as well as those cases in which infancy has been free from all symptoms of pyloric stenosis, but in which the symptoms appeared months or years later.

At the outset of this study one is immediately impressed by the fact that while medical literature is crowded with articles on congenital hypertrophic pyloric stenosis and pyloric spasm in infants, there has been, as far as I am aware, little written exclusively on the condition in older children.

The discussion in all of these papers deals with the problem as to whether the condition is congenital or not; as to the cause of the hypertrophy of the circular muscular fibers at the pylorus; as to whether in a given case the condition is one of pyloric spasm simply, or hypertrophic stenosis simply, or both spasm and hypertrophy, and as to the necessity for an operation.

The etiology of these congenital or early cases of pyloric stenosis has been considered as due, perhaps, to gastric hyperacidity, or at least to some disturbance of gastric secretion and consequent gastric indigestion. Other causes are hyperplasia at the pylorus, edema of the mucous membrane of the pylorus and pyloric spasm. The causes of spasm are not clear. It may be due to a toxemia, to gastric dilatation, to a change in the gastric secretion, or it may be nervous in origin. The classical symptoms are vomiting, constipation, progressive loss in weight, scanty urine, visible peristaltic waves, and possibly finding a tumor at the pylorus.

The treatment ordinarily advised is, feeding, stomach-washing, opium, poultices to epigastrium, saline enematas for the purpose of absorption of liquid, nutrient enemata, operation.

A study of the subject of organic pyloric stenosis as found in American, English, German and French literature has impressed forcibly on me the belief that a careful clinical examination of children and young adults will result in bringing to light a fair proportion of cases of organic stenosis during this period of life. The condition was long overlooked in infants; and while not flattering to clinicians, it is, I believe, nevertheless true that the condition is now being overlooked in the older child and young adult.

Children and young adults[1] who present gastric symptoms that continue for months or years, and especially if vomiting and epigastric pain are present, may be suffering from organic pyloric stenosis, and if such patients have been treated for a long time medicinally without benefit, the probability of there being organic pyloric stenosis increases. Many such cases have finally come to operation, and a pyloric stenosis found by the surgeon at operation.

The reason why medical treatment failed in these patients is then clear. Permanent changes have taken place in the gastric secretory apparatus, the result of the long continuance of the hypertrophic stenosis, and a cure by medical treatment is impossible. An early recognition of the pyloric obstruction should in a fair, or probably in a large, proportion of these cases lead to their cure by medical rather than surgical treatment. This seems at least probable, if one is to reason by the results obtained in pyloric stenosis in infants and older children. A study of the cases in infants and older children treated medically, shows conclusively that the majority of those infants who suffer from a mild degree of hypertrophic pyloric stenosis are cured by the physician and do not come to operation. Heubner[2] reports nineteen cured in twenty-one infants; Bendix[3] thirty in thirty-two cases; Hutchison[4] thirteen in fourteen cases. Stark[5] eleven out of twelve cases; Bloch[6] six patients, all recovered.

I do not wish to be understood as implying that there are not patients who require operation. I believe that the position taken on the question of operation by Robert Hutchison,[4] "that operation is never in any circumstances justified in these cases," is an extreme one, but that most of the cases of slight and moderate pyloric stenosis can be cured by medical treatment is my firm belief.

It is an accepted fact that many patients live into advanced adult life, who at autopsy show congenital pyloric stenosis. Rudolph Mayer[7] reports thirty-one such cases. Cautley and Dent[8] report three cases of pyloric stenosis at the age of 6, 11 and 22 years, respectively, and believe they were probably congenital. Mayo Robson reports one case, Lauderer[9] ten and William Russell[10] three cases.

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[1] Maylard: Brit. Med. Jour., July 11, 1908, p. 71.
[2] Heubner: Therap. d. Gegenw., 1906, viii.
[3] Bendix: Med. Klin., 1909, vi, 1813.
[4] Hutchison, Robert: Clin. Jour., Sept. 9, 1908.
[5] Stark: Zentralbl. f. Kinderh., 1909, xiv, 5.
[6] Bloch: Jahrb. f. Kinderh., 1907, lxv, 317.
[7] Mayer, Rudolph: Virchow's Arch. f. Path. Anat., 1885, cii, 413.
[8] Cautley and Dent: Tr. Roy. Med. and Chir. Soc., 1902, lxxxvi.

There is probably no doubt that congenital pyloric stenosis of a mild grade may remain latent for months and probably for years, and cases of organic pyloric stenosis have been observed during the second and third years of life, where a distinct insufficiency of motility, together with hyperacidity existed. There is probably hardly any year between early infancy and well advanced old age that does not show cases of pyloric stenosis in which the patients have come to operation. Some of these patients have had gastric symptoms from childhood; in others the symptoms vary from a few months to a number of years. Rosenheim[12] reports a case in a child who had always enjoyed good health until an attack of measles at the age of 5 years, from which he made a good recovery. Three months later the child began to vomit and continued to vomit almost every day. When 6½ years of age he was operated on and found to be suffering from hypertrophic pyloric stenosis. The case ended in recovery. Osler reports a case of hypertrophic pyloric stenosis in a child that lived until the third year.

There is much room for thought in the study of the cases in which the hypertrophic stenosis is not sufficient in amount to produce dangerous symptoms in infancy. The hypertrophy gradually increases in amount, the stenosis becomes more marked, and in later years the child presents the symptoms directly and indirectly produced by the stenosed pylorus. Beardsley reports a case at the age of 4 years, Sonnenberg one at 5 years, and Hansy one at 11 years (Cautley[13]).

Then there are cases that present exactly the opposite picture. The symptoms of hypertrophic pyloric stenosis are very severe in infancy; the babies are so ill that it seems as if they must surely die. They recover, however, and at the age of 3 or 4 years are apparently perfectly well. Robert Hutchison has reported such cases.

The question naturally arises, what has occurred in these cases? Has the congenital hypertrophy of the pylorus largely or partly disappeared? Has the compensatory hypertrophy of the stomach muscles been sufficient to overcome the original condition, and has no gastric dilatation occurred, or has it been a combination of both conditions? Cases are reported in which apparently no gastric dilatation has occurred, and the evidence in such cases points strongly to absorption of the hypertrophy.

What is the explanation of the very large percentage of recoveries reported by certain observers — Heubner, Bendix, Hutchison, Stark, and

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[9] Lauderer: Tübingen, 1879.

[10] Russell, William: Brit. Med. Jour., July 11, 1908.

[11] Bernheim (Zurich): Deutch. med. Wchnschr., 1908, p. 1830.

[12] Rosenheim: Berl. klin. Wchnschr., 1899, xxxii, 703.

[13] Cautley: Diseases of Children, 1910, p. 264.

Bloch? I believe it is as follows: Many of these cases are instances of pyloric spasm; others are cases of slight hypertrophic pyloric stenosis; in still others, both spasm and a mild degree of hypertrophy exist, and if one is ready to admit that a slight amount of hypertrophic pyloric stenosis may be largely or in part absorbed, the explanation is quite satisfactory. Stiles, who has operated on many of these patients, claims that true congenital hypertrophic stenosis of the pylorus is rare, and when it does occur, should be treated surgically. Cautley is of about the same opinion, but believes that very mild cases of this disease may recover under medical treatment. Cases of this character may, and probably do, in some instances, show gastric symptoms and evidence of pyloric stenosis in later life, since persistent stenosis in the older child is represented by, first, a period of compensatory stomachic muscular hypertrophy; this is followed by a period which may exist from the inception of the stenosis which represents stagnation and the slow emptying of the stomachic contents; and lastly, retention, or the failure of the stomach ever to completely empty itself. Is it not possible to recognize these cases clinically? Should they come to operation undiagnosed?

The following conclusions in regard to hypertrophic pyloric stenosis in older children and young adults seem to me to be justifiable:

1. Pyloric stenosis is present in children and young adults more commonly than is supposed.

2. The age at which it manifests itself depends on the degree of stenosis present.

3. Pyloric stenosis may be latent for years.

4. It is found by the surgeon during childhood and young adult life, and its early recognition by the physician is important from the standpoint of early medical or, if necessary, surgical treatment.

5. The entire disappearance of all the classical symptoms of congenital hypertrophic stenosis, and the apparent health of the infant during its subsequent early childhood, suggest the probability of an absorption of the hypertrophy, especially as no gastric dilatation may develop later in life.

CASE REPORT

It may be interesting in this connection to give the history of a case of pyloric spasm in a boy aged 6½ years, whose general health during infancy and childhood had been first-class until a few months before his death; who presented during the last few months of his life a typical picture of pyloric spasm; who came to autopsy, and in whom no disease of the pylorus or stomach was found post mortem.

History.—W. L., aged 6½, was admitted to the Jefferson Hospital March 8, 1911, under the care of Dr. Nassau, and I was asked by Dr. Nassau to see him a few days after his admission. The history of the case was as follows: Mother, father, two sisters, and two brothers were in good health; no hereditary history.

The child had pertussis one year previously. The left eye was injured by a fall in July, 1909, and the eye was enucleated in November, 1910; he gained 9 pounds in three weeks after the operation. Six weeks previous to admission to Jefferson Hospital he began to vomit. Vomiting occurred at irregular periods, bore no relation to the taking of food, and was most frequent in the morning. Vomiting was preceded by nausea and restlessness, which was relieved by vomiting. Vomiting might be absent for several days. He had no pain, no blood in the vomitus; had been rapidly losing weight, and was becoming much weaker, and had been confined to bed for one week. There was no history of chills or fever.

Examination.—The patient was poorly nourished; pupil of right eye was large, but reacted well to light and accommodation; a few submaxillary glands were palpable on both sides; tongue coated, with clean, pink margins. Chest poorly developed; ribs prominent; lungs normal. Abdomen was scaphoid; walls thin; no areas of tenderness or rigidity; no pyloric tumor could be felt. Urine, acid, 1,010, no albumin, no sugar, no acetone or diacetic acid; urea 2.9 per cent.; few leukocytes; no blood, no casts. March 17, 1911, the child had vomited three times in the previous two days; no vomiting had occurred during the two days previous to that; there was constipation; weight with night clothes and sandals, 35¾ pounds. The mother stated that he weighed 57 pounds two and one-half months previously. Report on the vomitus showed no hyperacidity and that bile was present. March 20 a bismuth meal was given. An *x*-ray plate seven hours after the meal showed the bismuth distributed in the stomach, but no trace of bismuth in the duodenum. This plate proved conclusively that food failed to pass normally from the child's stomach in the usual period, as a normal stomach will clear itself of a bismuth meal in from five to seven hours. Another plate showed the gold ball which had been placed in the orbit after enucleation of the eye. I did not learn until afterward that the eye was removed for sarcoma. The stools were small, yellow and well digested. The amount usually vomited at one time was never much more than the amount taken at one feeding. The Morro test was negative.

March 21. The child vomited first Jan. 20, 1910. The vomiting gradually got worse; formerly there was less effort in vomiting, but now vomiting was more violent and retching. He had been constipated all his life. The patient took and retained 14 ounces of water; no tumor was palpable with the stomach so distended. Examination of the unoperated eye showed no lesion of the fundus. The pulse was 130 to 150; temperature 97 F. to 102 F. The treatment consisted of liquid nourishment, nutrient enemata, stimulants, bromid of soda and alkalies. As the patient was not improving under medical treatment, and there was evidently from the *x*-ray plates a growth developing in the eye that had been previously operated on, and especially in view of the fact that I had learned that the eye had been operated on for sarcoma, a second operation on the eye was performed by Dr. Howard Hansell March 25, 1911.

Operation on the Eye.—The orbital cavity was completely filled with a dense hard growth, irregular in outline and extending forward to the commissure. The overlying conjunctiva appeared to be healthy. In operating for the removal of the growth, a horizontal incision was made through the conjunctiva from one canthus to the other. Through this opening the finger was introduced and by manipulation the tumor was enucleated and removed in sections. The largest portion included in its center the shrunken sclera, which partly enclosed a gold ball which had been inserted at the time of the enucleation of the globe some months previously.

The floor of the orbit was extensively necrosed and communicated by a large rough-edged, round opening with the antrum of the same side. The floor and outer wall of the orbit were denuded of periosteum, and contained several necrotic areas. The sphenoidal fissure was much larger than normal, by reason of adjacent diseased bone.

The patient rallied fairly well from the operation, but continued to grow weaker; vomiting continued; the amount of nourishment taken was very small, and he died April 6.

Necropsy.—Post-mortem record of W. L. Date of post-mortem, April 7, 1911, 12 noon.

Pathologic Diagnosis.—Sarcoma of liver, enlarged mesenteric lymph-nodes.

External Examination.—Body is that of an extremely emaciated male child. The left orbit contains a small quantity of gauze, which is saturated with purulent material. Rigor mortis present but easily broken up. Post-mortem suggillation is marked posteriorly.

Internal Examination.—Musculature wasted and subcutaneous fat very scant.

Peritoneum: Smooth and glistening; cavity contains a small amount of clear, straw-colored fluid; liver extends to costal margin, mid-clavicular line. The intestine is partially collapsed; this condition to be described later.

Left Pleura: Free from adhesions; surfaces are smooth and glistening; cavity contains a small amount of straw-colored fluid.

Right Pleura: Resembles its fellow of opposite side.

Pericardium: Smooth and glistening; cavity contains small amount of clear serum.

Heart: Normal in size. Right auricle—endocardium smooth and glistening; cavity filled with semifluid blood.

Left Ventricle: Wall is 0.6 cm. thick; musculature red and firm; cavity filled with semifluid blood.

Left Lung: Crepitates throughout; cut surface pinkish-red in color, and shows no gross lesions; weight, 160 gm.

Right Lung: Same. Weight, 150 gm.

Spleen: Measures 6x3x2 cm., is soft and of purplish-red color; weight, 160 gm.

Left Kidney: Measures 6x3.5x2.5 cm.; red in color; cuts with normal resistance; cortex bears normal relationship to pyramids and is red and injected; capsule strips readily, revealing a smooth surface; weight, 75 gm.

Right Kidney: Resembles its fellow; weight, 70 gm.

Ureters and Bladder: Show no gross lesions.

Stomach: Contains a small amount of yellowish material; capacity of 175 c.c. The mucous membrane shows some slight post-mortem discoloration. The pyloric orifice is patulous, and the pyloric ring seems to be normal in thickness.

Duodeum: Mucosa bile-tinged, but shows no macroscopic lesions.

Liver: Normal in size, reddish color, capsule smooth, cuts with normal resistance. In the right lobe near the anterior margin there is a firm, yellowish nodule measuring 4 cm. in diameter, sharply demarcated from the surrounding liver tissue. Remainder of organ apparently normal.

Pancreas: Normal in size and color, and shows no noteworthy lesions.

Intestines: Mesenteric lymph-nodes are enlarged, firm and of reddish color. The small intestine at a distance of 20 cm. from the ileocecal junction is collapsed for a distance of about 50 cm. Remainder of organ shows no lesions.

Vena Cava and Aorta: Normal.

Microscopic Diagnosis.—Tumor of Liver: Small round-celled sarcoma.

Pylorus: Normal.

Mesenteric Glands: Hyperplasia of lymphoid tissue.

Brain: Showed nothing.

The case of pyloric spasm here reported and coming to autopsy is to me of great interest. It was unconnected with any organic disease of the stomach, or with any change in the normal gastric secretion. Spasm of the pylorus in older children is spoken of by many authors, and is usually described as being associated with severe pain, perhaps little or no vomiting, and often connected with disease of the pancreas, appendix or gall-bladder, gastric ulcer, or distinct change in the gastric secretions. Pain was absent in my case; vomiting was the one prominent symptom, and loss in weight was rapid and extreme. In these two particulars, absence of pain and violent and persistent vomiting, it differs from the cases described by most writers. After the enucleation of the eye, the vomiting lessened, and in three weeks the boy gained 9 pounds. The vomiting ceased for five or six weeks after the first operation, and then gradually increased in frequency and severity until the second operation, when the sarcomatous mass was thoroughly removed from the orbit.

The case appears to belong to the group of so-called nervous vomiting, of reflex origin, associated primarily with disease of the eye, and later, aggravated by metastasis in the liver. Reflex vomiting of eye origin is independent of the taking of food, and while it lasts is persistent. The vomiting of eye origin does not last for days, and is usually followed by an ability to take and retain food. The primary operation was followed by entire cessation of vomiting, and a gain in weight. The sarcoma returned in the orbit, metastasis occurred in the liver and both these conditions caused, in my opinion, a severe return of this gastro-neurosis. The operation of cleaning out the orbit only slightly affected the vomiting; the boy was in a deplorably weak condition at the time of the operation, and the sarcoma of the liver was probably instrumental in causing a continuance of the vomiting, which persisted, although in a less degree, until his death. In my opinion, the second operation neither hastened or retarded death.

The stomach through the sympathetic and cerebrospinal nerves is connected with practically all organs and tissues in the human body, and it has been demonstrated that pyloric spasm can be produced artificially by stimulation of the vagus. The contraction of involuntary muscular tissue, the source of the contraction being outside the stomach, is at least probable.

Is pyloric spasm unassociated with pain and with persistent vomiting, a common condition, or even an occasional condition in older children? It certainly clinically does not resemble the cases described as associated with gastric ulcer,[14] and gall-stone colic in which the pain is excessive and vomiting not a marked symptom. Periodic pyloric spasm may occur at the menstrual period,[15] unassociated with any disease of the stomach, or with spasm in any other portion of the body, and under such conditions is probably a primary spasm of the pylorus, a motor neurosis. Lauder Brunton's observations tend to show that pyloric spasm may accompany migraine, and be a manifestation of a neurosis.

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[14] Fairchilds: Iowa Med. Jour., Des Moines, 1910-11, xvii, 212.

[15] Hemmeter: Diseases of the Stomach, Ed. 3, p. 744.

A number of cases of infantile pyloric spasm have been followed up to the age of 5 years and older, and found to be in first-class health, and a neurotic family history is not found in quite a considerable number of such cases. The clinician should not lose interest in these babies after they pass beyond the period of infancy, and an effort should be made to follow their subsequent histories, especially with reference to any gastric symptoms.

Cases of infantile pyloric spasm have been kept under observation for years.[17] All the symptoms may persist until the third year, and the child may remain nervous and anemic for years afterward. In other cases, solid food cannot be given until the child is 3 or even 5 years old. In still other cases of spasm, vomiting may persist until the child is 4 years old or older, and the peristaltic waves may continue until the child is over 4 years of age.

Cases diagnosed as cyclic vomiting have come to autopsy[18] and the lumen of the pylorus has been found to be very small, with a distinct hypertrophy. In these cases the children may be 4 or 5 years of age, the symptoms of epigastric pain and vomiting having been present since birth, returning at irregular intervals of months, and the children being apparently perfectly well between the attacks.

I do not mean to give the impression that cyclic vomiting and pyloric spasm are not two entirely different conditions, but to suggest the advisability of considering the possibility of pyloric spasm producing symptoms that resemble closely those of cyclic vomiting.

What are the causes of the pylorospasm in infancy that disappears in later childhood? Half of these children are breast-fed, and it seems to me unnatural to claim, as does von Starck, that the unaccustomed presence of food in the stomach produces an irritation of the gastric mucosa and so causes the spasm.

A clearer understanding of the etiology in infants may help us in the recognition and study of the condition in older children.

1713 Spruce Street.

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[16] Von Stark: Zentralbl. f. Kinderh., May 1, 1909.

[17] Heubner: Berlin, Therap. d. Gegenw., 1906, viii, 433.

[18] Russell: Proc. Roy. Soc. Med., London, 1909-10, iii, Sect. Dis. Child., 78.

AN APPARATUS FOR THE COLLECTION OF THE EXCRETA OF INFANTS *

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NEW YORK

The collection of the excreta of male infants is not a difficult matter. All that is necessary is to immobilize the child's pelvis, adjust the proper receptacles and let nature take its course.

Many kinds of apparatus have been used for this purpose and there is quite an extensive literature on the subject. This is well reviewed by Schabad[1] and by Langstein,[2] who also describes the technic of the investigation of the problems of the metabolism of children. Most of the devices for collecting urine go back to the girdle and test-tube principle of Raudnitz.[3] The devices for holding the child in one position have their origin in the hammock principle of Bendix,[4] modified later by Bendix and Finkelstein.[5] The hammock is tied to the ends and sides of the crib and the child fastened with his body resting on a support made of pillows, his legs spread apart and immobilized, his buttocks slung free over a dish or rubber cloth and his penis placed in a tube which leads to a glass

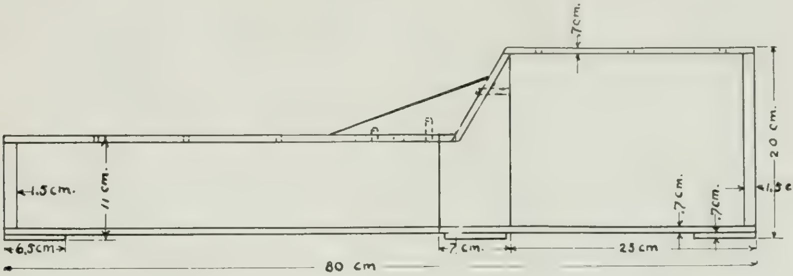

Fig. 1.—Diagram of apparatus for holding infants in metabolism experiments, showing measurements and method of construction.

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*From the Pathological Laboratory of the Presbyterian Hospital and the Department of Applied Pharmacology, Cornell University Medical College.

*Demonstrated before the Section on Medicine New York Academy of Medicine, May 17, 1910.

1. Schabad, J. A.: Arch. f. Kinderh., 1908, xlviii, 402.
2. Langstein, Leo.: Handbuch der biochem. Arbeitsmethoden, 1910, iii, 1016.
3. Raudnitz: Prag. med. Wchnschr., 1883, viii, 359.
4. Bendix, B.: Jahrb. f. Kinderh., 1896, xliii, 23.
5. Bendix and Finkelstein: Deutsch. med. Wchnschr., 1900, xxvi, 672.

receptacle. An American modification by Talbot[6] makes use of a Bradford frame with a round hole for the buttocks.

A limited experience with several of these devices showed that it was necessary to use a good deal of restraint and a good deal of vigilance or the baby would get out of position. The child, although he was really warm and comfortable, looked chilly and uncomfortable. This roused unfavorable comment from nurses, parents and visitors. The apparatus of Howland and Cooke[7] is free from most of these disadvantages and does its work with absolute accuracy. It is easy to make and is perfectly comfortable for the baby, but has the disadvantage of being attached to the crib. This makes it bulky and hard to move and also somewhat conspicuous to anxious parents. Still it is probably the most convenient form of apparatus for much of the work done with children.

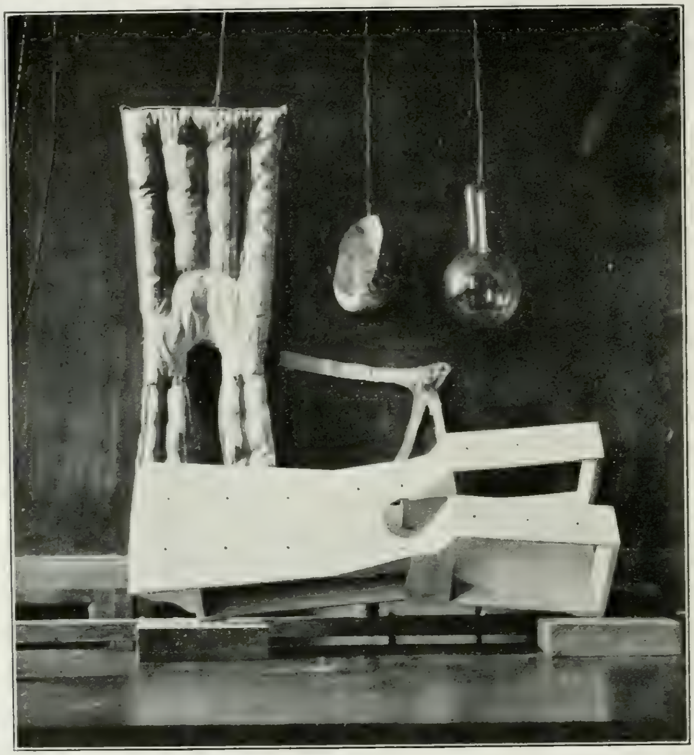

Fig. 2.—The complete apparatus, including mattress, receptacles for holding feces and urine and the girdle for holding the latter.

From the necessities of my work I was forced to make an apparatus (Figs. 1, 2 and 3) which was portable and inconspicuous. It seemed

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6. Talbot, F. B.: Jour. Am. Med. Assn., 1909, liii, 1818.

7. Howland, J., and Cooke, R. A.: Am. Jour. Dis. Child., December, 1911.

desirable also to keep the baby with thighs flexed, as this is the natural position for infants and is the position adopted in most of the recent devices. A frame of wood covered with a mattress was therefore modeled to fit the baby with thighs flexed. An inclined plane under the thighs prevented downward motion, a cloth band over the thighs prevented upward motion and a rounded trough in which the pelvis lay, prevented lateral motion. Beneath the buttocks was an opening with a receptacle for feces. Between the legs there was ample room for the neck of a flask to hold the urine.

The babies did well on this bed and seemed to enjoy the additional attention and the entire absence of wet diapers. The whole affair was so small that it could be placed in a bassinette and so flat that no one would suspect the child was restrained in any form of apparatus. It could be easily wrapped in a blanket and carried outdoors or held in a mother's lap while the infant nursed. When the proper receptacles were used, there was absolutely no loss of urine or feces. I have never seen children kept more than three days on the apparatus, but there is no reason why the period should not be extended. There are very seldom any pressure signs.

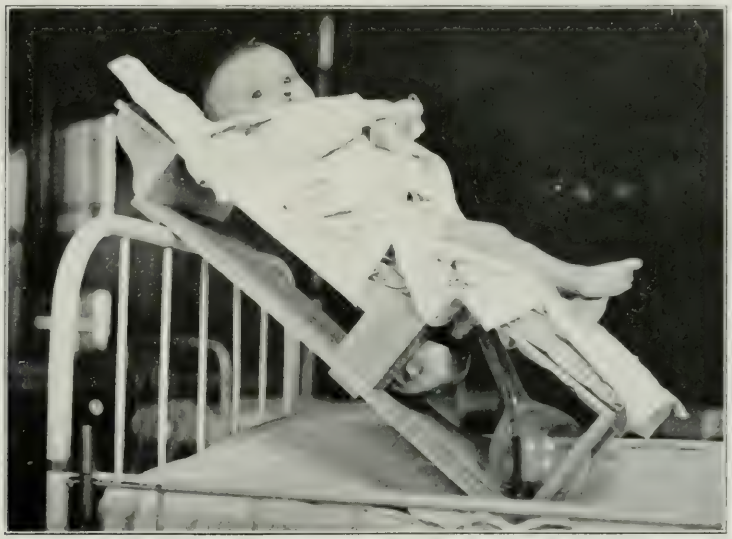

Fig. 3.—The apparatus assembled and the infant secured in place.

The accompanying pictures show the construction of a frame which will hold children weighing up to 8 kilos (17½ pounds), but is somewhat large for very young babies. It is made of light wood 0.7 cm. in thickness, and is carved so as to fit the pelvis and buttocks. White enamel paint makes the best finish. The mattress should be about 5 cm. in thickness and should be securely bound to the frame by strings passing through the holes bored in the top of the frame. It is particularly important to have the mattress form a good hollow for the buttocks. The edges of the hole under the buttocks should be protected by sewing a dress shield to the mattress. The best feces receptacle is a sugar scoop with the handle cut off, attached by a wire to a hook on the under surface of the frame. Instead of the sugar scoop a deep enamel-ware cup may be used.

The girdle for the urine receptacle is shown in the photograph. A thick-lipped test-tube which fits comfortably over the boy's penis is bent, drawn out and cut off at the constricted portion. This is passed through the hole in the girdle and secured to it by means of a wire. To protect the scrotum, the penis is passed through a hole in a square piece of non-absorbent cotton, is smeared with vaselin or boric ointment and placed in the test-tube. The girdle with its leg bands is then adjusted and the test-tube arranged so as to empty into the neck of a large flask. It is better not to use rubber tubing if it can be avoided. In the flask should be placed a crystal of thymol to prevent decomposition of the urine. The flask is easily suspended from the under surface of the frame by wires. The urine flows better if the head of the frame is raised a little.

To hold the child on the frame one should use broad cloth bands around the thighs and around the abdomen. This lets the baby kick his legs, wave his arms and wriggle his thorax and neck. It is wise to put a pillow on either side of the frame to help keep the child from wriggling too far.

The frame and mattress can be made at a cost of about eight dollars. Once made it lasts indefinitely and can be used for many babies. I have not tried to use it with female infants and have not yet tried it in surgical cases which demand restraint.

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A METABOLISM BED FOR INFANTS*

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The following is a description of the metabolism bed that we have used during the past two years. It is very simple and comfortable and gives excellent results. For this reason it is described.

The bed proper is one in general use in New York. It is made of iron, with a movable spring mattress, which may be raised or lowered at the head or foot (Fig. 1). During experimental periods the foot of the mattress is lowered at a decided angle as shown in the picture. A stout frame, made of half-inch gas-pipe, 16 inches wide and 3½ feet long, is allowed to rest on the mattress at the head of the bed and is fastened firmly to the bars so that it will not slip toward the foot. Below, the frame is suspended by straps or tape to the sides of the crib so that the foot is slightly lower than the head. This inclination is of advantage in making the collection of urine and feces easier, and the slight tendency of the child to slip toward the foot is of assistance in holding him in a proper position. The greater angle at which the mattress is inclined leaves a space between the mattress and the frame in which the receptacles for the collection of urine and feces may readily be placed.

The upper part of the frame is covered by a piece of stout canvas about 16 inches wide, drawn very tightly and smoothly and laced on the under side of the frame.

A special retaining sheet is cut as shown in the diagram (Fig. 2). Its size must depend somewhat on the size of the infant used for study. In general the hole for the buttocks should be 5 inches in diameter and those for the legs 3 inches. The upper part of the sheet is torn to form strips, like the ordinary scultetus binder. The last strip should come a little below the level of the hole for the buttocks, as this holds the buttocks more firmly in place. The holes in the sheet are faced with canvas on the under side and strips of canvas are continued down the sheet to a point a little below the level of the leg holes in order to strengthen the sheet at the places of maximum strain. The sheet is roughly stitched to the canvas covering of the frame, care being taken to have the hole for the buttocks about 2 inches below the lower end of the canvas. A wooden bar is fastened across the bed to the side of the crib just above the lower end of the canvas.

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*From the First Medical Division of Bellevue Hospital, Children's Service

The child is prepared as follows: A woolen jacket protects the body. Cotton is bound about the knees to protect them from pressure by the leg holes, and in cold weather the legs and feet may be completely covered by cotton held in place by gauze, with stockings drawn over all, or the infant may be dressed in a woolen night dress with legs.

Male babies only can be used. The penis is placed in a glass or metal tube, held against the symphysis by a rubber waistband with perineal straps and connected with the collecting flask below by rubber tubing. Glass tubing has proved most satisfactory for the penis as it can easily be varied in size and shape, is readily cleaned and allows one to see that the position is proper.

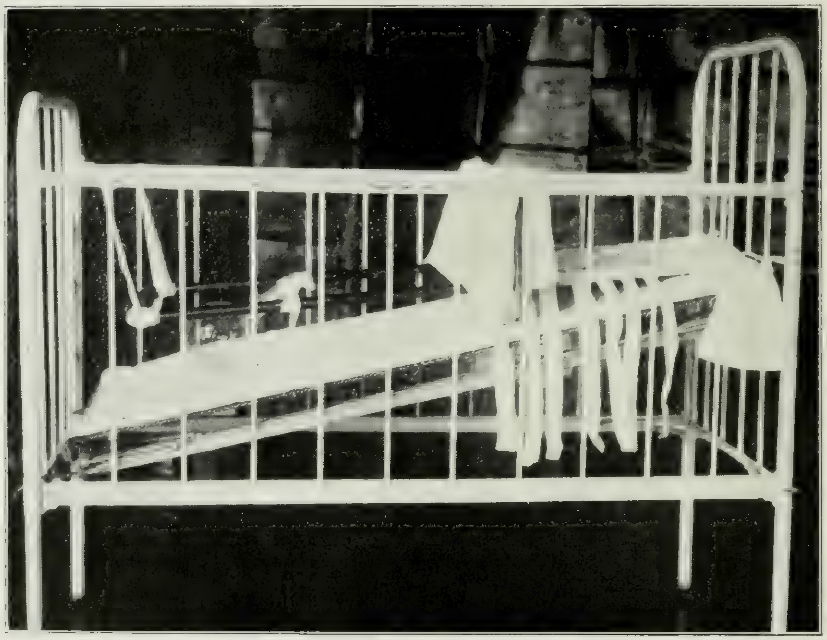

Fig. 1.—Metabolism bed, showing position of spring mattress frame, collecting flask, etc.

The child is then placed on the frame, the legs drawn through the leg holes to the knees, the buttocks well down in their proper hole, and the scultetus binder is loosely tied. The lower part of the sheet is then drawn up to the cross bar and pinned or tied as shown in the diagram. The feet are supported by a hammock of gauze swung across the bed parallel to the cross bar and a little below it. A large porcelain dish is put under the buttocks and the tube from the penis is placed in the glass flask fastened in the frame as shown in the picture. Pillows or blankets are then placed around the inside of the bed to protect from draught, and hot water bottles, if necessary, may be added.

A satisfactory metabolism bed must be simple, efficient and comfortable. The frame and sheet of the bed described above are easily made and it takes but five minutes to put a child on the frame. We can also vouch for the efficiency of this bed. But above everything, the comfort of the patient must be provided for, for only in this way is a normal, or rather, representative, metabolism maintained. It is particularly this feature which has commended this bed to us above the many others described. The child lies in a perfectly natural position with slightly flexed thighs and with absolute freedom of the arms and legs, and these are at all times supported so that he can move them at will or allow them to lie still without any strain on them. He can, moreover, turn somewhat from side to side, if the binder is loosely tied, without the risk of disturbing the collection of excreta.

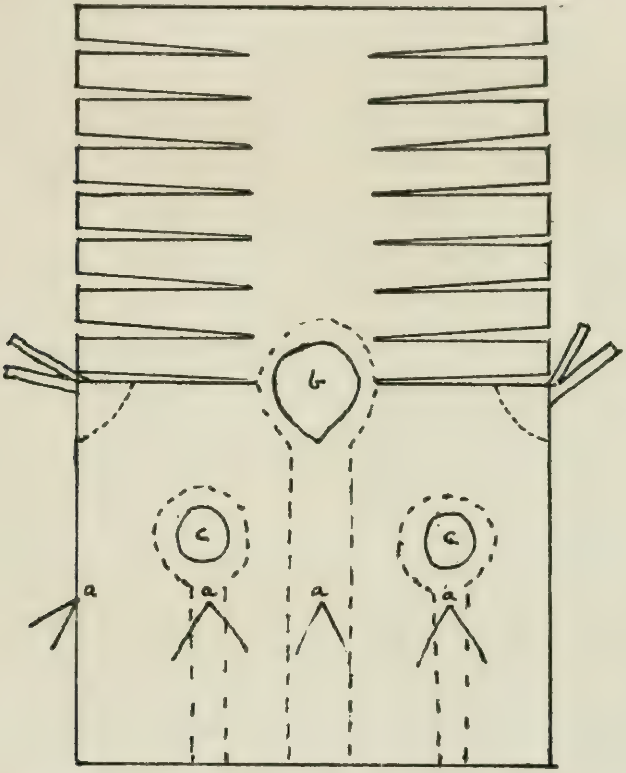

Fig. 2.—Diagram of bed sheet. Dotted lines show reinforcement with canvas; a, tape for tying to cross-bar; b, hole for buttocks; c, holes for legs.

We have kept infants for days on this frame without the slightest evidence of fatigue or resentment at restraint.

24 West Fiftieth Street.

PROGRESS IN PEDIATRICS

DISTURBANCES OF NUTRITION OF THE ARTIFICIALLY FED INFANT WITH PRACTICAL APPLICATION OF THE CLASSIFICATION OF FINKELSTEIN

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CHICAGO

In order to make the subject more comprehensible, I take the liberty of reviewing the etiology of nutritional disturbances as classified by Langstein and Meyer.

ETIOLOGY IN GENERAL OF NUTRITIONAL DISTURBANCES

VARIETIES

1. Food qualitatively normal, but metabolism abnormal. Idiosyncrasy, as seen in (1) neuropathic infants; (2) exudative diathesis.
2. Milk infected with bacterial products due to the action on fats and sugars. (These products are not affected by sterilization.) Seen most in (a) summer, and (b) unhygienic milk.
3. Primary infection. Dysentery, typhoid, streptococcus enteritis, etc.
4. Secondary infection. Probably primary injury of the sensitive intestinal epithelium, a counterpart of the nephritis which is so frequently seen following colds, pharyngitis, otitis, pneumonia, pyelitis, cystitis, etc., in sick infants.
5. Inanition, as seen in (a) pyloric stenosis; (b) excessive starch feeding (*Mehl-nahrschaden*).
6. Overfeeding. Not necessarily based on an excessive fuel value of the ingested food, but frequently due to a preponderance of one or more food elements, either alone or in the presence of a vitiated digestive apparatus.

It is the latter problem, i. e., *overfeeding,* which we will discuss, referring to the previously named etiologic factors only in so far as they may directly have a bearing on the cases under discussion.

HISTORY

The history is of vast importance in all nutritional disturbances and worthy of the most careful consideration. The following should be carefully noted: the constitution of the child, with the presence of hereditary and developmental defects, a neuropathic history, or the presence of an exudative diathesis; lowered immunity, as evidenced by previous general, local, or gastro-intestinal infections; history of improper feeding; quality or quantity of individual feedings and total food taken, and the frequency and number of feedings, with notation of the resulting effect on weight and temperature curves. Briefly stated, in a normal child an increase of food results in increased weight, normal temperature, and normal stools; while in nutritional disturbances increase of food results in decreased weight, increased temperature, and often abnormal stools, a paradoxical reaction.

The effects of the individual food elements in excess in nutritional disturbances are as follows: *Salts* cause a rise in temperature; *sugars* cause toxic symptoms, rise in temperature, and diarrhea; *fats* cause toxic symptoms, obstipation and usually fat stools (possibly diarrhea); *proteins* cause no corresponding findings. Results are not due to the individual ingredients, but to their relations to each other in a given food.

Based on the above etiologic factors and metabolic facts, Finkelstein has divided nutritional disturbances into the following types:

I. Disturbed metabolic balance (Bilanz Störung).

II. Dyspepsia.

III. Intoxication.

IV. Decomposition (acute atrophy).

Nutritional disturbances should not be considered as local intestinal lesions, but as general, deep-seated disturbances of the whole organism.

I. DISTURBED METABOLIC BALANCE (BILANZ-STÖRUNG — FINKELSTEIN; MILCH-NÄHRSCHADEN — CZERNY-KELLER; ATROPHY OF MODERATE DEGREE)

1. Exogenic Factors.— Improper nourishment (usually excess of fat in food). Under this head we will consider in detail the disturbances described by Czerny-Keller under the name of *Milch-Nährschaden* (nutritional disturbances due to excessive milk feeding), which usually arise during the course of feeding with ordinary milk mixtures, the clinical picture usually being due to the fat content, which may be relatively or absolutely in excess.

2. Endogenic Factor.—Congenital idiosyncrasy toward milk digestion. This is clinically characterized by

(1) *Weight:* Notwithstanding proper or even excessive caloric intake, there may be no gain in weight or an irregular increase, however, under the normal.

(2) *Temperature:* Varies as to the causative factor. Usually we find a daily oscillation from 1 to 2 degrees, with a tendency toward subnormal. However, in the presence of associated excessive carbohydrates there is an early hyperpyrexia due to the development of dyspepsia. This is especially true of infants under six months.

(3) *Stools:* In excessive milk feeding (*Milch-Nährschaden*) the common type is the fat soap stool, which is dry, light in color (gray to white), friable, and does not stick to the napkin. In the presence of excessive carbohydrates this stool may be lacking, due to the presence of a slight dyspepsia.

(4) Regurgitation and vomiting are frequent.

(5) Skin is pale, with loss of elasticity.

(6) Muscles are soft and flabby.

(7) Abdomen tympanitic.

(8) Child restless.

(9) Sleep disturbed.

(10) Immunity lessened, with resulting furunculosis, eczema and intertrigo.

(11) Urine usually shows no marked changes.

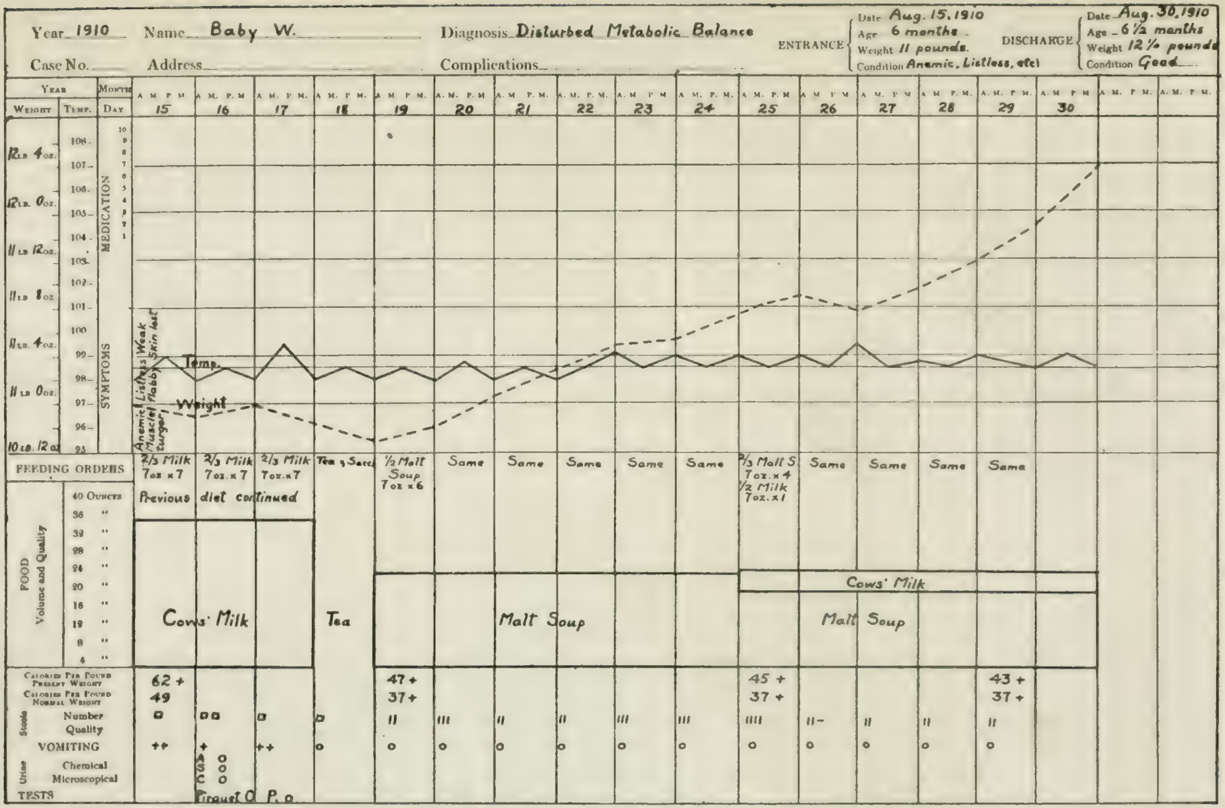
Metabolism.—A careful study of the relative intake and the excretion of the individual constituents of milk shows us that

(1) Protein digestion and retention are normal.

(2) Fat absorption, according to Freund, is normal. Other substances, which result in the formation of an alkaline reaction within the intestines, will lead to soap stool formation. A substance which does this is casein. This is indirectly shown by the feeding of casein to breast-fed children with dyspeptic stools, which become less frequent and alkaline. The watery stools seen in artificially fed children receiving whey are often quickly improved by adding casein to the diet (Finkelstein); and in well children by adding casein even in moderate quantities an increase in the alkali salts and calcium are seen in the stools.

Fat only in the presence of certain products of food, therefore, leads to the formation of fat soap stools. The presence of fat soap stools is of importance in showing that an excess of fatty acids have been combined with Ca and Mg, but it does not prove that the presence of these stools indicates at all times a pathologic loss of Ca and Mg, as it may only be a relative, and not an absolute, loss. The above illustrates the error of Czerny's conclusions that fats *per se* are the cause of fat soap stools, which Finkelstein claims are due to loss of salt balance. Therefore, the conclusion of Czerny that fat soap stools constitute a symptom of poor fat absorption, with loss of body fat as an end result, is an error. However, an analysis of the stool fat constituents, i. e., neutral fat, fatty acids and soaps, shows an abnormal relation which is of importance. Normally 18 per cent. of the total fat constituent in the stools consists of the insoluble Ca and Mg soaps, of which, in disturbed metabolic balance, approximately 48 per cent. are insoluble Ca and Mg soaps; therefore, it is evident that there is an excessive calcium and magnesium waste through the stools.

Paradox Weight Phenomenon.—Salts other than the calcium and magnesium do not seem to be markedly affected by this negative balance, evidenced by the presence of soap stools. Fat soap stools can only be viewed as of importance in disturbances of nutrition when the Ca balance is pathologically changed. The reversing of the Ca balance results in stationary weight. Nutritional disturbances due to excessive milk feeding are the result of too much earthy alkali being thrown off through the bowel and the organism being robbed of its acid-binding radical, and, therefore, the organism must call on the ammonia radical to neutralize the same. This is evidenced by the presence of the increase of the ammonia coefficient in the urine, i. e., the relation between the ammonia and the total nitrogen products. This phenomenon, discovered by the Czerny school, is especially marked in intoxication and decomposition. The above findings apply to disturbed metabolic balance described by Czerny under the title of *Milch-Nährschaden.* Much less is known of the metabolic changes in the nutritional disturbances due to excessive flour feeding (*Mehl-Nährschaden*). Weigert believed in the latter, that the organism becomes richer in water and salts and poorer in the dry substances. Of the metabolic changes due to infection nothing is known.


Year 1910 Name Baby W. Diagnosis Disturbed Metabolic Balance

Case No. Address Complications

ENTRANCE Date Aug. 15, 1910 Age 6 months Weight 11 pounds Condition Anemic, Listless, etc.

DISCHARGE Date Aug. 30, 1910 Age 6 ½ months Weight 12 ½ pounds Condition Good

Fig. 1.—Chart showing hospital record of an infant with disturbed metabolic balance.*

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*A brief description of the clinical sheet used by me may be of value, as it answers both the needs of a history sheet and daily chart as well. The points illustrated by it are, a graphic relationship between the temperature, weight, quality and quantity of food taken, and the end-results on the stools and urine. Also separate spaces are provided for complications which may influence the preceding under the heading of symptoms, together with spaces for treatment other than dietetic, energy value of foods, vomiting, blood examinations, tuberculin reactions, etc. Gummed slips in six colors, representing different foods used in our wards (human and cow's milk, buttermilk, albumin milk, malt-soup, chymogen-milk) are used to graphically illustrate the quality of food given, the quantity being represented by cross-lines on the colored slips, corresponding with the 4-ounce spaces on the chart. The small figures 1-10 are used to make an electrical reaction curve in cases showing a spasmophilic diathesis.

DIAGNOSIS

The diagnosis of disturbed metabolic balance is based on the history of

1. Food of sufficient caloric value.
2. No gain in weight.
3. Slight variations in temperature.
4. Absence of acute symptoms, but a general loss of turgor.

To condense descriptions of stools and urine, the following characters are used:

STOOLS: | = normal; / = soft; — = quite soft; m = watery; [] = fat soap; x = mucus; c = curds; bl. = Blood.

URINE: A = albumen; S = sugar; Ac. = acetone; D = diazo; I = indican; C = casts; P = pus; Bl = Blood.

PROGNOSIS

The *prognosis* is usually good, even in the artificially fed.

TREATMENT

Change the causative diet. Reduce the quantity of milk and add carbohydrates, or substitute milk low in fats, usually skim- or buttermilk, and add malt or other easily assimilable sugars. In young infants human milk is by far the best form of feeding. The good results of treatment are due to the fact that the tolerance for carbohydrates is not reduced.

1. Diet With Human Milk.—This is by all means the best treatment, especially in young infants. Weight increase may be slow at first, probably due to low salt and protein content of human milk. A loss of more than 6 to 10 ounces over a period of three or four days is frequent. More than this should lead one to suspect an error in diagnosis. This loss may be due, as stated, to stopping of a food rich in proteins and salts, and substituting one low in the same with the continued excretion of water through the kidneys, bowels, etc. This stage is passed in about four days and the system adapts itself to the new ingredients. Other symptoms which must not lead to error are paleness, loss of turgor and sinking cheeks which soon disappear with beginning weight increase. Temperature and pulse do not change, and the stools assume a breast-milk character. If the stage of reparation is slow, and the child does not gain in weight, the substitution of one meal of food rich in protein and salts daily will frequently help (buttermilk or skim-milk). Mother's milk also helps to increase immunity.

2. Diet with Artificial Foods.—In the pathogenesis of feeding of milk, fat plays the most important rôle, and this is best counteracted by replacing it by the well-tolerated carbohydrates. In simple cases reduce the quantity of milk and add carbohydrates, estimating the form of sugar and starches, and if this does not answer, or if the quantity of milk in the previous diet was not too great, then change the kind of sugar. The following answer in most cases: (1) Soxhlet's *Nahrzucker* (nutritional sugar). (2) Cane sugar. (3) Mellin's food. (4) Horlick's malt food.

SEVERER CASES

1. Malt soup (Keller) (laxative), made as follows, is exceedingly valuable:

(1) Milk 11 ounces warmed gradually; add flour 1⅔ ounces; stir constantly, then pour through gauze filter; (2) malt extract (Trommer's, etc., will answer)

3 ounces; boiled water, 22 ounces; potassium carbonate solution, 10 per cent., ⅓ ounce; (3) mix both solutions. Put on slow fire, stir continually, and boil for two or three minutes. Caloric value 800 to the liter. Formulæ: fat, 0.5 per cent.; protein, 2 per cent.; carbohydrate, 12 per cent. This can, at first, be diluted, if indicated. This food should usually be changed after two to four weeks. Loeflund's and Borcherdt's Malt-Soup Extracts do not require the addition of the potassium carbonate solution.

It is indicated in the presence of fat soap stools which soon become pasty and of a mahogany brown color; best between 3 and 6 months; after 6 months add more milk to increase the protein. It is contraindicated below 3 months, if the stools are loose.

2. Buttermilk and skim-milk plus sugar and flour (two carbohydrates). (Antilaxative; action both the same.)

(1) Indicated especially in infants under 3 months.

(2) Valuable over 6 months because of high albumin content.

(3) In convalescence they fill the needs of albumin hunger.

(4) Antilaxative because proteins cause a rich intestinal secretion, which results in putrefaction, which tends to constipation.

(5) Contraindicated in fat soap stools (less valuable than malt-soup in clearing them up).

Human milk diet may cause an early loss of weight because of low salt and protein. Cow's milk diet causes an early, rapid gain in weight due to fixing water in the tissues by increased salts and carbohydrates. Fat rich food causes loss of earthy alkali salts through bowel, resulting in soap building and loss of weight by loss of body salts. This must be counteracted by carbohydrates which increase weight by allowing the organism to use more salts. The early rapid increase is later equalized by the organism and soon becomes less rapid.

General symptoms following change of diet are, better sleep; improved turgor; skin less pale; less variation in temperature. Stools change from soap stools to (1) buttermilk, yellow-brown, alkaline, and fair consistency; (2) malt-soup, acid, softer, mahogany-brown color.

The above changes are due to the protein and carbohydrate constituents.

The results of treatment are due to the fact that the tolerance for carbohydrates is not lessened. Study each case to see if excess of carbohydrates is not being given which is indicated by (a) restlessness; (b) stopping of weight increase after early rise; (c) increase in number, acidity, and amount of mucus in stools; (d) alimentary fever (irregular). If there is irregular fever, human milk must be substituted.

The above mixtures should be gradually replaced by milk-mixtures after two to eight weeks.

OTHER THAN ORDINARY TYPES OF DISTURBED METABOLIC BALANCE

1. The ordinary type, already described (*Milch-Nährschaden*), due to excess of fat.

2. Infections, as otitis, pharyngitis, cystitis, etc. This form readily yields to the same treatment as 1 after cessation of infection.

3. Excessive carbohydrate nourishment (*Mehl-Nährschaden*) is only seen in older children with broader carbohydrate tolerance; in young infants dyspepsia is an early result with excessive carbohydrate feeding.

Treatment consists in administering milk mixtures, i. e., foods high in fat.

II. DYSPEPSIA (STADIUM DYSPEPTICUM OR STAGE DYSPEPSIA)

In practice, especially in young infants, frequently we do not see the stage of disturbed metabolic balance, but see dyspepsia directly, due to an excess of sugar in the food. This can be likened to an excess in whey components when milk is the food used. Fats, unless in excess, probably only play a secondary rôle due to the presence of sugar fermentation. This is characterized clinically by acute gastro-intestinal symptoms, the most marked of which are the stools, which are increased in number and of an abnormal quality. The organism does not show signs of any deep-seated general changes; weight loss is moderate or remains constant, temperature is moderately increased and repair is rapid with the withdrawal of the improper food.

The diagnosis can only be made by a careful consideration of the history, the clinical and functional symptoms, and only that picture of gastro-intestinal findings which developed primarily in a healthy infant or follows directly the stage of disturbed metabolic balance can be diagnosed as dyspepsia and treated as such; otherwise cases of intoxication and decomposition may be neglected.

ETIOLOGY

1. Congenital lowered tolerance to cow's milk.
2. Errors in diet with milk of good quality. (a) Overfeeding with diet of normal proportions (too frequent and too much). (b) Feeding with a diet of improper proportions (excess of sugar, etc.).
3. Feeding with infected milk.
4. Infection of the gastro-intestinal tract (external infections).
5. Systemic infections (otitis, pharyngitis, etc.) associated constantly with a lessened tolerance for food.

SYMPTOMS

Symptoms in General.—Severe symptoms are absent. The mind is clear. The heart action is not rapid. Respirations are not greatly increased. The skin remains unaltered.

Weight.—If there is an excessive sugar feeding in the treatment of a preceding disturbed metabolic balance, we at first get an increase in weight. This ceases later, and dyspepsia develops with moderate weight loss.

The temperature is irregular and moderately increased, and, when it follows diets rich in sugar and salts, is of the alimentary type.

Gastro-Intestinal Symptoms.—The appetite is poor. The mucous membrane of the mouth is red and may be the seat of thrush (due to decreased immunity). Vomiting may be present and usually occurs long after feeding. The stomach may contain food seven to eight hours after feeding, which contains volatile fatty acids (odor), but no free HCl. The abdomen is distended and peristalsis increased (auscultation). Restlessness is marked, probably due to abdominal findings.

Stools.—The clinical diagnosis is usually made from the stools. They are increased in number and watery, and the reaction is usually acid.

The color is green, mucus is present, and curds composed of fatty acids, not casein, are present. The number is more important than the quality, as microscopic examination gives us little etiologic or therapeutical enlightenment, and we cannot get a very definite idea of the quantitative chemical contents.

Bacteria specific for dyspepsia are unknown.

Urine.—Sugar, albumin and casts are absent, unless there is a tendency toward intoxication.

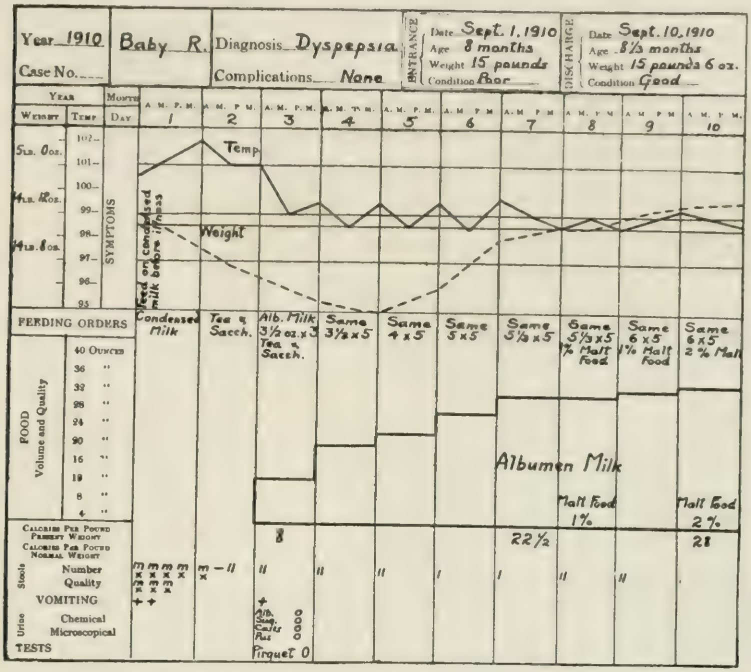

Fig. 2.—Chart showing hospital record of an infant with dyspepsia.

METABOLISM

Changes in part are due to (1) peristalsis; (2) to increased intestinal secretion, which latter accounts for the moderate increase in the protein matter in the stools, and not, as formerly thought, to decreased digestion of the food proteins (casein, etc.). The remainder of the curds is due to fatty-acid salts and bacteria. Fat absorption is usually only slightly reduced. Fat diarrhea is not frequent and only seen in fat-rich foods.

Soaps and neutral fats are in about normal relation to the total fat content. Volatile fatty acids formed from carbohydrates and fats by bacterial action are increased. Sugar is absent. Starch varies directly with the peristalsis. Salts in stools are increased. Green color is usually due to oxidation of bile constituents.

In general, protein retention need not suffer. Ash balance may remain normal. The water in the stools is increased, and in the urine is decreased.

PATHOGENESIS

Sugar and salts, which in the normal child cause no symptoms, in the impaired organism, or in excess, can cause dyspepsia, as evidenced by diarrhea and fever.

Pyrogenic Action of Food Constituents. Action of Salts.—Sodium is the most important salt in raising temperature. Meyer gave a normal child 100 c.c. 10 per cent. NaCl solution per mouth, with usually no result, but in infants with gastro-intestinal symptoms the temperature was raised. Potassium is less important in raising temperature. Calcium rather tends to lower temperature. The mode of action is unknown.

Sugar.—Milk-sugar is more active than malt-sugar in raising temperature, but sugars are less constant experimentally than salts. Whether due to sugar itself or products of fermentation is also unknown. *Proteins* cause no rise in temperature and tend to improve stools. *Fats* have an uncertain and probably indirect action. (They seem to add to the bad effect in the presence of sugar and salt disturbances which, however, cease when the latter are withdrawn.)

The dyspeptic picture is due to (1) slight intestinal epithelial injury following various causes; (2) the administration of certain foods: (a) whey and sugar, which are the most important, and (b) fats, of less importance. These must be administered in quantities large enough to affect the injured epithelium and further impair its function, but not sufficient to cause intoxication.

PROGNOSIS

This is good with proper diet. It is bad with improper diet, with tendency to intoxication and decomposition, varying indirectly with the age of the infant and directly with the previous number of attacks and tendency to recurrence.

TREATMENT

Human Milk.—The younger the infant, the more indication there is for human milk.

Artificial Food.—Remember that primarily the sugar and whey content of the food, and, secondarily, the fats are the irritants.

1. In mild cases reduce the milk to a minimum, and especially the sugar content.

2. In the severer cases reduce the sugar, whey and fats. It is best temporarily to withdraw food entirely as follows:

(1) Starvation (or hunger) for one day (tea and saccharin).

(2) Indifferent diet for second day (low in food value and salts); i. e., Young, one-third milk (best boiled) plus two-thirds thin oatmeal gruel, without sugar. In severe cases, one-third skim milk plus two-thirds thin oatmeal gruel without sugar. Buttermilk may be used in place of milk. The quantity on the second day should not exceed 6 to 8 ounces, as follows: five feedings of 1 to 1½ ounces of food, and 20 to 25 ounces of tea, plus saccharin, given *ad libitum*, giving a total of about one quart of fluids. This will usually answer. Further treatment depends on the reaction to the above; if the general appearance improves, also the disposition, etc., and the weight loss ceases in two or three days (which is the case even in under-feeding), then the treatment was correct, otherwise decomposition must be thought of.

(3) When the weight-curve is constant, the quantity should be increased, but the quality left unchanged; 5×2 ounces, etc., of the same mixture, plus water or

tea to the necessary quantity between the feedings. Weight increase should not be expected because of the low sugar content, but a decrease in weight should always be considered serious.

The stools are, at first, small and contain mucus; later less frequent, and often on milk mixtures without sugar there are fat soap stools which are a good indication.

3. If the temperature and stools are normal after three to five days, carbohydrates can again be added, best in the form of malt preparations (avoid milk-sugar because of its rapid fermentation), beginning with 1 per cent., and gradually increasing to 5 per cent. At first, there is a rapid increase in weight; later a slower one.

Avoid under-feeding too long, even if the stools look bad, if the temperature and weight curves improve, because of the danger of decomposition. Fats can be added in place of sugars, but this should be done with care. (Experiments with cod-liver oil have given me the best results.)

ALBUMIN MILK[1]

The albumin milk of Finkelstein is distinctly indicated in these cases.

Direction for Making: To 1 quart of milk previously boiled for five minutes in a double boiler, add 1 tablespoonful of chymogen (elixir rennet, junket tablets, dessert-spoonful of pegnin or tablespoonful of essence of pepsin). The dish containing the milk is now placed in a water bath, and the milk is heated to 107° F.

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[1] Directions for making, recently obtained from the Kinder-Asyl diet kitchen, are as follows: To 1 quart of raw milk add 1 tablespoonful of essence of pepsin (elixir rennet, junket tablets, dessertspoonful of pegnin or chymogen) and stir for one-half minute. The mixture of milk and ferment is now kept at 100 to 107 F. and perfectly quiet for about fifteen minutes, when the clot is formed. The free whey is now poured off and the remaining curd is put into a thin muslin bag, or one made of four layers of gauze (if too thick it drips too slowly or vice versa, curds will pass through and some of the curd is lost), and left to drip for one hour. The curd is now placed in a fine hair sieve and rubbed through with a potato masher, adding buttermilk, one pint, to facilitate this process. The passing through the sieve should be repeated until the curd is minutely divided.

Now, as a final process, water to make a total mixture of 1 quart and 1 per cent. of malt-sugar are added.

This is now put into a receptacle resembling a small ice-cream freezer and put on the stove to boil for ten minutes. While boiling, the handle is vigorously turned, stirring the milk inside thoroughly and constantly (stirring with an egg-beater if the above is not obtainable will answer; the former is to be recommended as it also prevents evaporation. I find that stirring with a spoon does not cause agitation enough to prevent large curd formation.)

Churning is continuously kept up for two reasons: 1. To make the curd finer. 2. To get the suspension more homogeneous. After ten minutes of boiling, the kettle is placed in a bath of cold water to cool it off, still turning the crank for a few minutes until the milk is cool. Then it is put into bottles. Overheating for feeding ruins the product; 100 F. does not change it.

[NOTE: With all due courtesy to the author we wish to state that the first method of preparation was adopted in our diet kitchen, because of the indefiniteness of the details in its preparation as first published and the consequent difficulties encountered in attempting to get a fine curd.]

for thirty to thirty-five minutes. It is now put aside for fifteen minutes, then the excess of whey is poured off and the remaining curd is put into a thin muslin bag, or one made of four layers of gauze (if too thick, it drips too slowly, or if vice versa, curds will pass through and some of the curd is lost), and left to drip for two hours. The curd is now placed in a fine hair sieve, any further free whey drained off and then rubbed through with a potato masher, adding buttermilk 1 pint to facilitate this process. (The buttermilk used is made from whole milk heated to 180 F. for forty minutes, then cooled to 80 F. The scartaline is now added, and after standing from eighteen to twenty hours at the latter temperature it is churned to remove the butter-fat.) The passing through the sieve should be repeated until the curd is minutely divided. Now, as a final process, boiled water to 1 quart is added, and 1 per cent. of malt sugar is added. Sohxlet's Nährzucker is used for my cases, although Mellin's food or Horlick's malt food answers the purpose. Therefore, the finished product contains the curd from 1 quart of boiled milk and 1 pint of boiled buttermilk, 1 pint of boiled water, and 1 per cent. malt sugar.

I have found that rubbing the curd through the sieve with buttermilk prevents the freeing of fat from the curd, so frequently seen when water is used. Boiling the milk, although freeing somewhat less whey, makes only a moderate difference in the quality of the end product, and in our cases has been much better taken by the infants than that made from whole raw milk with its heavier curd which requires shaking during feeding.

Albumin milk prevents abnormal fermentation in the intestinal tract on account of (1) the low content of easily fermentable milk sugar; (2) the low content of whey salts (the latter favor fermentation), and (3) the comparatively high protein content (the latter counteracts fermentation). On standing, a precipitate is likely to form in the bottle containing the albumin milk. Before feeding, the bottle should be well shaken. The quantity to be fed should be warmed to the body temperature and again shaken. Overheating is objectionable. The milk should be kept in a cool place. If thus taken care of, it preserves its quality well, for at least five weeks.

Albumin milk contains 3 per cent. protein, 2.5 per cent. fat, from 1 to 1.5 per cent. of milk sugar, 0.5 per cent. of mineral salts. The mixture contains 450 calories to each liter (Finkelstein). My own tests show the fat content somewhat lower, averaging about 2.2 per cent.

Directions for Use.—Albumin milk is indicated in all infantile disorders which are associated with diarrheas, especially in those cases in which breast milk is not obtainable. It is also valuable in cases of dyspepsia, entero-catarrh, cholera infantum (intoxication, Finkelstein), acute atrophy (decomposition, Finkelstein).

In cases even where the bowel movements continue thin and frequent, or contain mucus, one should proceed to make a daily increase in the quantity of albumin-milk, and after a lapse of eight days begin to add more sugar, or even sooner if the stools warrant it, gradually increasing the dextrin-maltose to a total of 5 per cent. If the weight still remains at a standstill, 2 per cent. of flour may be added. It sometimes happens during the period of convalescence, after improvement has once set in, that an apparently unfavorable condition occurs, characterized by frequent and thin stools. In these cases it may be said with great emphasis that one should not diminish the quantity of the albumin-milk or the sugar, but should continue with the same dosage and quietly wait. After a short time, if this suggestion is followed, improvement usually sets in; however, when a profuse diarrhea is associated with a marked drop in weight, the sugar must be reduced.

In some of these cases the disturbance is not primarily a digestive one, but it seems to be associated with an infection in some other part of the body. Thus, for example, an intercurrent rhinitis, or bronchitis, will almost invariably cause a standstill or loss in weight, with more or less pronounced digestive disturbance.

Management in Detail.—In cases of dyspepsia, feed the baby tea sweetened with saccharin for six hours. Begin by feeding 300 gm. (10 ounces) of albumin milk, divided into five or six feedings. Tea and saccharin may be given between feedings, as seems indicated. This can be gradually increased by adding 50 to 100 gm. daily until 180 to 200 gm. per kilogram body weight are given. Carbohydrates should be added as previously stated. Children will usually require from four to eight weeks of treatment with albumin-milk. After this time appropriate milk mixtures should be tried. The change from albumin-milk to other mixtures must be made quickly and completely, all bottles being stopped at one time. Relapses are an indication for a return to albumin-milk.

(For further details for its use see intoxication and decomposition.)

Other Treatment.—1. Avoid laxatives (castor oil, calomel, etc.), except for an initial dose. 2. Avoid gastric lavage, at least in early cases. 3. Warm compresses to abdomen aid in removing flatulence, etc. 4. Astringents (tannigen, tannalbin, bismuth subnitrate) are indicated after the weight-curve is steady, temperature normal, and the child generally improved, but the stools still frequent.

III. INTOXICATION (ENTERO-CATARRH; CHOLERA INFANTUM)

This is characterized by violent gastro-intestinal symptoms, rapid loss in weight and other symptoms of deep-seated alterations in the functions of the organism. Collapse and nervous symptoms outweigh the intestinal symptoms. On these findings Finkelstein bases his nomenclature rather than on the intestinal findings, as in previous classifications.

ETIOLOGY

The causative factors are the same as for dyspepsia, i. e., excess of sugar and whey content in the food, but here we have a more severe picture. All factors which cause nutritional disturbances can cause intoxication, but the important point is, which moment in a nutritional disturbance leads to the phase of intoxication?

Factors in a Nutritional Disturbance Which Tend to Intoxication.—*1. Food.* (a) Combination of food elements which individually would be insufficient to cause a disturbance. (b) Infected food, i. e., spoiled milk. *2. Infection.* (a) Gastro-intestinal infection. (b) Systemic infections, as otitis, cystitis, pharyngitis, etc., by disturbing the digestive function. *3. Heat.* Heat can cause a chain of symptoms in itself resembling intoxication. All depends on the individual resistance, a more severe irritant being necessary in the disturbed metabolic balance, and dyspepsia, than in atrophy to develop the intoxication stage.

Carefully following nutritional disturbances teaches us that a definite constituency in the food leads to the various phases, e. g.:

1. Intoxication follows diet rich in sugar and whey content.

2. Decomposition (atrophy) follows diet rich in fat and relatively poor in sugar. These facts are so definite that one can prophesy which variety will prevail in a clinic by knowing the diet commonly in use (Finkelstein).

To develop intoxication there must be an injured intestinal epithelium or preexisting nutritional disturbance. Enteric and systemic infectious processes, as well as heat, give rise to intoxication through their action on the cells of the digestive apparatus in the intestines and the secretory digestive organs. Czerny and Keller believe much trouble is due to infected milk, not to the bacteria themselves, but their acids (toxins formed from fats and sugars by them).

SYMPTOMS

1. High temperature. 2 Rapid loss in weight, even 1 to 2 pounds in a few days, mainly due to loss of water. The skin becomes dry and inelastic. 3. The stools are liquid, are usually numerous and contain mucus and occasionally blood. 4. Collapse. The skin is gray in hue, eyes sunken with distant stare; pinched nose; also frequently incoordinate movements of the extremities, slow and often limited to one extremity; also catatonia of the extremities, and aimless movements, as of chewing, etc. 5. Typical respirations (deep, rapid without pause); described as "toxic respirations." 6. Glycosuria is almost constant, and the sugar is of the same variety as that in food. The phenyl-hydrazin test is the best as the copper sulphate tests require long boiling with lactose, etc., and the reaction may be overlooked. 7. The urine contains albumin and casts. The amount of urine is small, even to anuria. 8. Leukocytosis is present up to 30,000. 9. The heart action is weak, the pulse small and irregular. 10. Vomiting is frequent and the vomitus may contain blood. 11. Nervous symptoms may be pronounced and cause confusion with meningitis. The sensorium is disturbed (with an occasional cry as if in pain). The hydrocephaloid state may be present with strabismus, convulsions, etc. Whether uremia is a factor in this condition is very questionable. 12. Sclerema is constantly seen in the severer types, a very bad sign, due to a coagulation of tissue fluids of an unknown nature (Czerny-Keller).

METABOLISM

Clinical findings lead one to expect marked metabolic changes.

Protein.—Feces.—Nitrogen quota increased, probably due to increased peristalsis and intestinal secretion. Experiments are insufficient.

Urine.—There is a marked increase over the normal under same conditions as to food. During instituted hunger-day the albumin metabolism still progresses and is probably due to toxic processes. Changes from the normal end-products of protein metabolism are present. The ammonia coefficient is increased from 10 to 40 or 50 per cent. (Langstein and Meyer).

1. Change in amino-acids to urea (experiments with glycocoll-amino acetic acid) are interfered with and some excreted as glycocoll in the urine, probably due to a liver insufficiency (disturbance in synthetic production of urea) (Pfaundler). This theory of Pfaundler can also apply to the increased ammonia

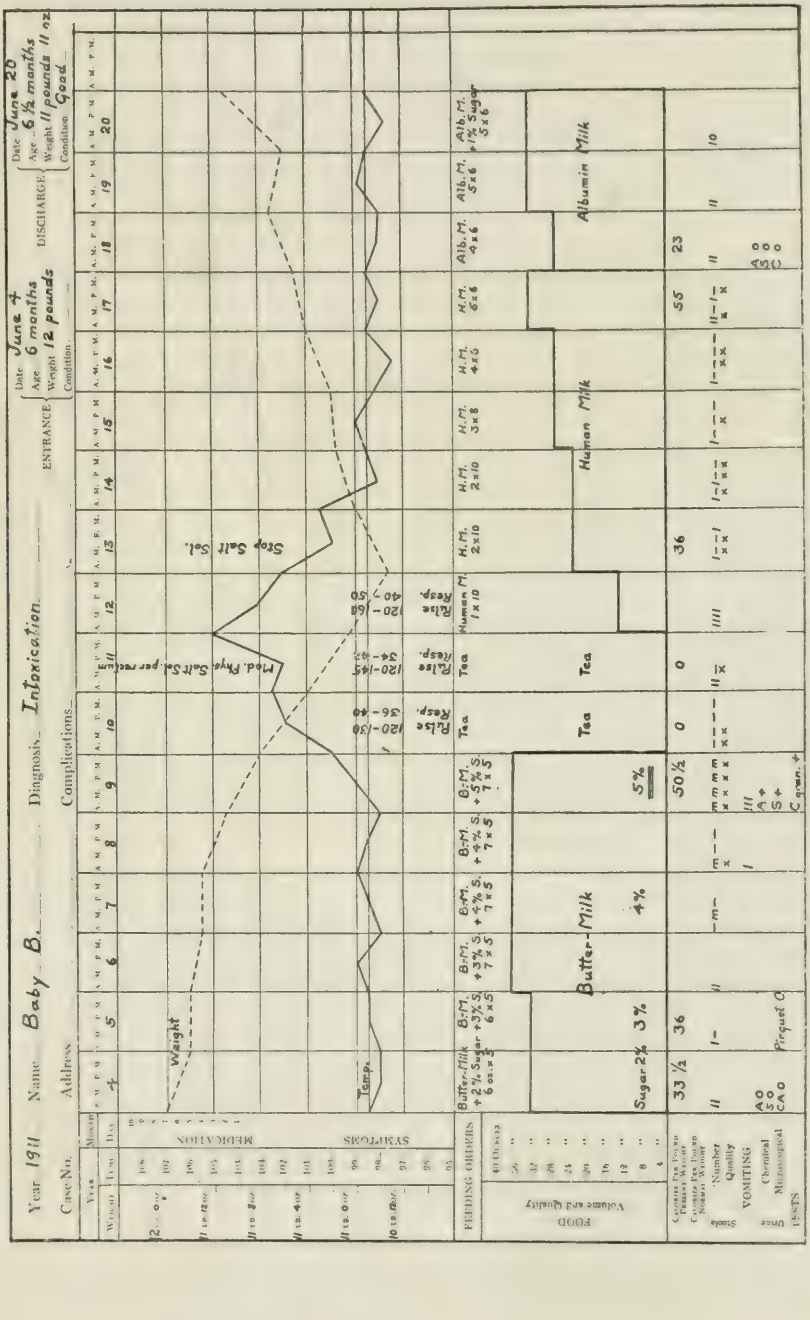

Fig. 3.—Chart showing hospital record of infant with intoxication.

coefficient other factors which probably positively cause increased ammonia coefficiency.

2. Removal through the intestinal tract of Ca and Mg to neutralize the temporary fatty acids, and necessitating the utilizing of ammonia to neutralize the normally formed acids in the urine.

3. The acids (acetone and aceto-acetic acid) formed during the starvation period (toxic) must be neutralized in the urine.

4. Due to interference with carbohydrate metabolism, the fats are not completely burned up in the system by sugar, and as a consequence the acids are combined with alkalies Na and K, and as these are not sufficient the excess is combined with ammonia in place of being thrown out as urea (Rosenstern). This is a typical diabetic reaction (Rosenstern).

Fat.—Meyer found absorption reduced from 97 per cent. to 60 per cent. This improves early in convalescence. Splitting of fat is bad and we get an acidosis with the presence of acetone and aceto-acetic acids (butyric acids, etc., Rosenstern).

Carbohydrate.—Sugars of the type ingested are seen in the urine long before the end of the proper assimilation period. This ceases when the sugar is withdrawn from the diet.

1. With milk sugar in the diet we get milk sugar and galactose in the urine, while other components, as glucose, are missing, on account of the fact that part of the milk sugar is absorbed unchanged, and as it cannot be used as such in the system, it is again excreted, probably due to the injured epithelium allowing it to pass through, and not to the absence of the lactose ferment which Langstein and Steinitz always found present.

The presence of galactose is due to a different cause, and indicates that there is an insufficiency in the sugar oxidation function, and the system is only able to burn up the glucose. This is a liver insufficiency. Other disaccharids have the same ending. Maltose differs from these only in that it can be burned in the system as such without previous splitting in the bowel; therefore, its presence in the urine is double evidence of a lowered power of oxidization by the organism; that is, in its intermediary metabolism.

Water.—Great loss in weight is probably due to the loss of water. Water is lost in the urine and stools which, however, together have been found to equal about the normal amount, only the proportion is inverted, the bowels excreting the greater portion. Loss in body weight is, therefore, in all probability, due to excessive loss (pathologic) through the skin and lungs. Respiratory experiments must prove or repudiate this.

Salts.—(No good experiments to date). Excesses of salts are excreted in the stool, especially the chlorids. There is a negative balance of Cl. It is questionable whether the salt loss is the primary cause of the water loss, or whether the loss of water by the system has its own pathogenesis; indeed, it would require a great salt loss to account for the great loss of water, and it is quite possible that a toxic influence results in a disturbance of the water-binding property.

RELATION OF INTOXICATION TO FOOD ELEMENTS (FINKELSTEIN)

We are able with regularity in dyspepsias to produce intoxication by continuance of the carbohydrate and whey-rich foods; also in light cases to improve by withdrawing carbohydrates alone: in severer cases by withdrawing both carbohydrates and whey elements.

INTOXICATION IN COURSE OF INFECTIONS

Pathogenesis is not due to a single factor. We know that some are influenced by food withdrawal; others are not. 1. We must believe that the infection injures the intestinal wall and other digestive organs. 2. From this point pathogenesis is the same as in alimentary intoxication. The toxic influences of different infections are as different as are the infections.

PATHOLOGY

In the small intestine there are usually no marked changes. Hyperemia of the mucous membrane and enlarged follicles, especially Peyer's patches, are usually present. Liver, cloudy swelling and fatty degeneration (probable causes of insufficiency). Rott and Tugendreich have believed that an acidity (*Saurung*) of the liver and muscle tissue is present.

DIAGNOSIS

The diagnosis is based on the above symptoms, with improvement on withdrawal of food for twenty-four to forty-eight hours.

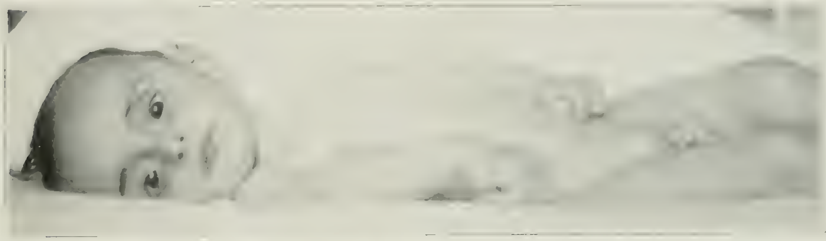

Fig. 4.—Infant with intoxication whose hospital record is shown in the chart Fig. 3.

PROGNOSIS

This depends much on reaction to hunger diet, as very severe symptoms disappear often in twenty-four to forty-eight hours. If the same do not disappear in twenty-four to forty-eight hours, in the absence of infection the prognosis is bad. Infections add to the severity. They are bad as a complication of chronic nutritional disturbances.

TREATMENT

1. Removal of all food with sufficient water administration.
2. In severer types, subcutaneous salt infusions twice daily, 100 to 150 c.c., even though there is danger of salt fever in the severer types.
3. Salines per rectum, best administered by the drop method. One drop per second for four hours is 400 c.c. One-half strength of the following solution is good:

	gm. or c.c.
$NaCl$	7.5
KCl	0.1
$CaCl$	0.2
Water	1000.0

4. One lavage, if food has been given shortly before.

5. Avoid all laxatives, as the bowels empty themselves; also avoid astringents.

6. Analeptics. Give a mustard bath; reddening of the skin is a good sign.

7. Antipyretics. Use cold packs, and leave the infant undressed.

8. Stimulants. Caffein sodium benzoate, gr. $^1/_{10}$ to ½, four or five times a day; camphorated oil, 1 c.c. every two hours, if indicated; epinephrin solution, 0.6 in 1,000 c.c. of salt infusion; veronal, gr. $^1/_{10}$ per dose, is less depressing than chloral.

9. Sedatives for convulsions, etc.

10. Diet: Hunger diet should be employed not longer than twenty-four to forty-eight hours. Occasional administration of dilute saline solutions (NaCl 5.0, $NaHCO_3$ 5.0, water 1,000), per mouth, also vegetable soups, Moro's carrot soup,[2] Eichel kaffe or thin soya-bean gruel, may soon be used with care, to supplement an occasional tea feeding.

Human Milk.—Human milk is by all means the best food. Feed often and in small amounts, ten times daily, 5 c.c. from bottle or spoon. The first milk should be fat-free. Increase when the temperature, etc., do not react to food, and then not more than 50 c.c. daily.

A sustaining diet should be reached in eight to ten days (32 calories per pound), after which the child can be put to the breast five times daily. If the elevation of temperature returns, except in the presence of infection, cut down the food. The gain in weight is very slow in the stage of repair on human milk, due to the low protein and salt content.

Cow's Milk.—For the first few days after the hunger diet, a food low in fat and sugar should be fed because of the lowered tolerance. One-half skim-milk or buttermilk mixture, without sugar, will answer, but should be fed in small quantities, 10 × 5 c.c. daily, then 10 × 10 c.c. On this low diet weight loss and temperature will usually stop. After ten to fourteen days, 32 calories per pound may be fed. Less rapid increase than in human-milk feeding should be the rule. Older infants can be given gruels in their milk. Recurrence of dyspepsia is an indication for return to indifferent food. With a second recurrence breast milk is absolutely indicated. Return to carbohydrates should be made with great care. Albumin milk is indicated in this condition, and the following is a good working rule for its use in these cases: First day, tea. Second day, 10 × 5 c.c. albumin-milk, with tea *ad libitum.* Then increase 50 c.c. daily until stools are good, then increase 100 c.c. daily until 180 to 200 c.c. is given daily for each kilo weight. After the stools are solid, add 1 per cent. of sugar to the food, and increase gradually to 4 per cent. In intoxication I have obtained better results by at first feeding albumin milk without sugar additions. In infants over 6 months 1 per cent. of flour can also be added. After six to eight weeks, an ordinary milk mixture can be fed. Feedings can now be reduced to five or six daily. Never feed over 1,000 c.c. a day of albumin milk.

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[2] *Moro's Carrot Soup.*—One pound carrots are peeled, sliced and cooked one to two hours, and after mashing, poured through a sieve and mixed with the bouillon made from a pound of beef and 1 liter water. To the latter add one teaspoonful of salt.

IV. DECOMPOSITION (ATROPHY: SEVERE TYPE: MILCH-NÄHRSCHADEN: SEVERE TYPE)

Bilanz-Störung may be the direct forerunner of decomposition if the dietetic error is not corrected.

Dyspepsia leads to decomposition if fat predominates in the food and sugar is not present in excess; otherwise we get intoxication. Czerny's internal hunger or cell hunger is the cause of decomposition, in contradistinction to hunger as usually thought of, which is due to lack of food to appease the appetite. It is characterized by general severe changes: (1) Rapid fall in weight; average 20 to 100 gm. daily loss, somewhat slower than in intoxication. (2) Lack of ability to assimilate food. (3) Subnormal temperature with irregular daily curve, with tendency toward collapse. (4) Slow and small pulse, with weak heart-tones. (5) Rapid respirations; prolonged expiration, and irregular breathing, even to the Cheyne-Stokes type. (6) The sensorium is not involved. (7) Urine contains no albumin or sugar. (8) Stools from normal to very bad, depending for their character on the previous diet. Dark brown stools usually indicate duodenal hemorrhages (Helmholtz). (9) The hunger is often very great and cannot be satisfied. (10) Vomiting is frequent

Only a determined effort to limit the diagnosis decomposition to such conditions as are associated with acute rapid loss of body weight (lowered temperature) and general disturbance of the normal body functions will lead us to get good results in our therapeutic applications. It should follow nutritional disturbances in whose pathogenesis alimentary toxins play the chief rôle, and should not be confused with the subacute and chronic atrophies, as tabes mesenterica (tuberculosis), etc.; neither is it to be confused with chronic disturbed metabolic balance, which can be differentiated by a functional diagnosis; that is, a test meal, as described later.

ETIOLOGY

All factors leading to dyspepsia and intoxication may be forerunners of decomposition. At what moment this change takes place can only be answered by the fact that deep-seated organic changes are necessary to its development; these changes which produce such an intolerance toward nourishment may have developed previously to the preceding illness or during its course. Premature infants are especially predisposed, also young infants with previous dietetic errors, and diarrheal attacks; also those fed on one-sided foods, especially carbohydrates, as cereal diets: and also from too long-continued hunger diet. Especially in the young does this apply to cereal waters. All of the preceding reduce the tolerance toward normal food and its assimilation. The tendency to decomposition and, therefore, to narrowing of the nutritional sphere increases with each dyspeptic attack. Death may also be caused by secondary infections, but be unrecognized because of a low temperature, cystitis, etc. (Alimentary sickness, with infectious death, Pfaundler.) Death may also follow quite normal stools without preceding symptoms of dissolution, but this is usually following some dietetic error with cardiac or respiratory failure. This is often the cause of sudden death in our service in malnutrition cases.

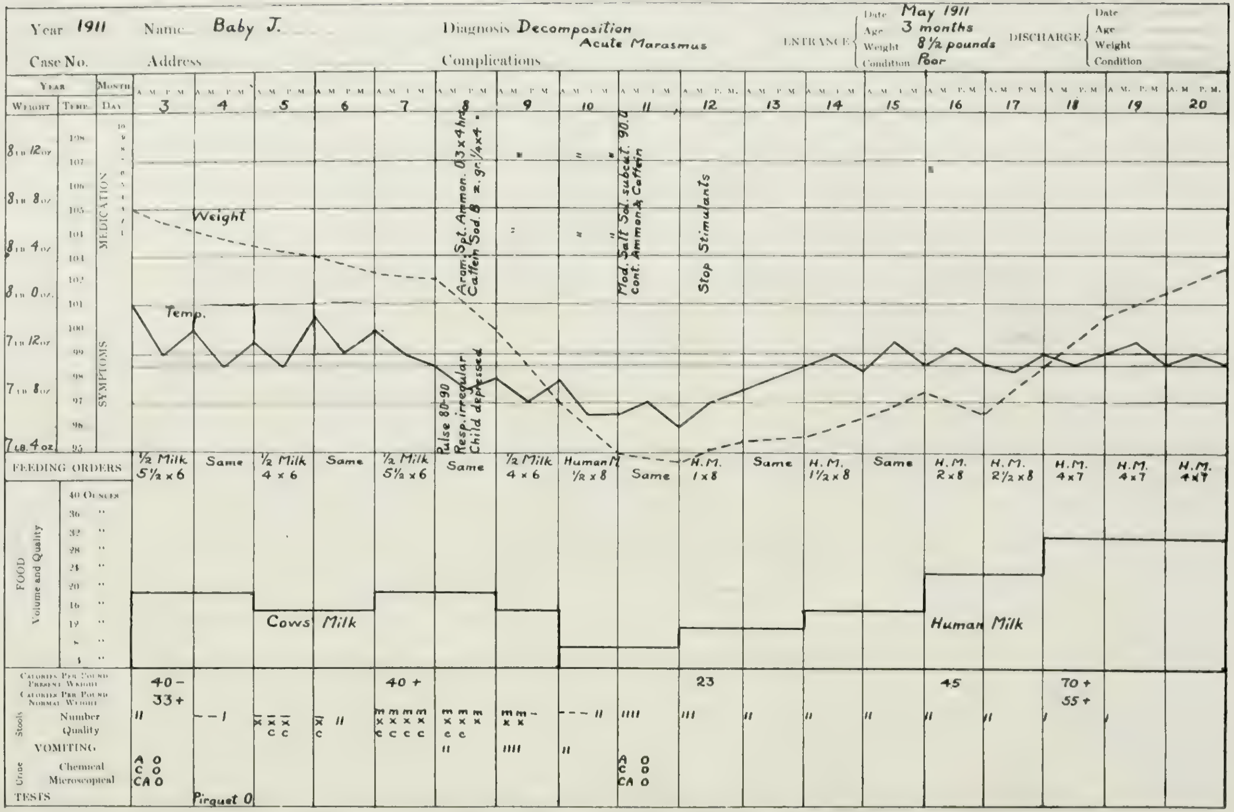

Fig. 5.—Chart showing hospital record of infant in Fig. 6 with decomposition.

DIAGNOSIS

We must ascertain the degree of nutritional disturbance, which is accomplished by noting the history from the present attack backward. If the case be a decomposition, we find an infant who has had a history of repeated diarrheal attacks, with a rapid loss in weight; improvement on hunger diet, with recurrence on refeeding, and a gradual decreasing of the assimilative powers to a point where supportive diet becomes impossible. This difficulty in the stage of repair with proper diet is absent in disturbed metabolic balance and dyspepsia. If this history fails, our only recourse is a very careful test for the reaction to hunger diet and food.

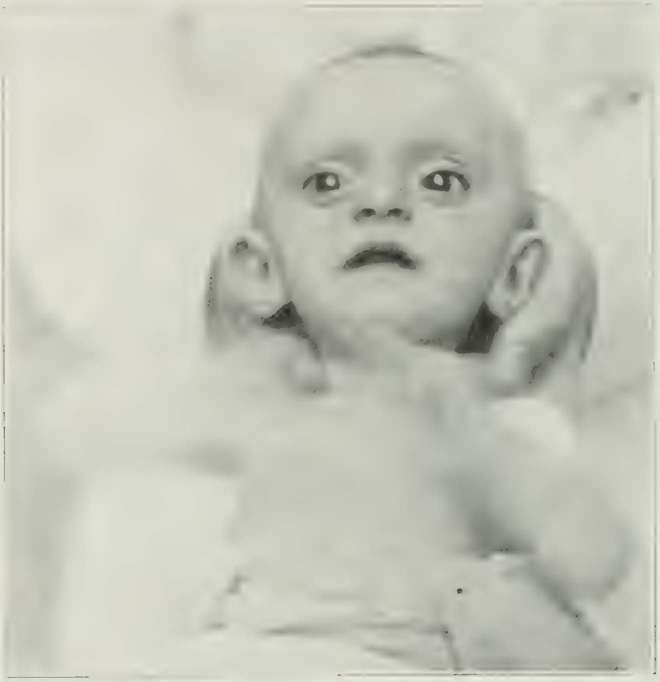

Fig. 6. Infant with decomposition whose hospital record is given in Fig. 5.

1. *Reaction to hunger diet* is always dangerous. (a) Temperature falls even to collapse. (b) Pulse also slows and weakens. (c) Weight always falls, but varies with the severity of the case. (d) Stools become more nearly normal.

2. *Reaction to food:* This gives a clew to the stage of which Finkelstein recognizes three. The first stage is very much like that of dyspepsia, except that there is a loss in weight with supportive diet. With careful diet the weight loss ceases in from three to six days. In the second stage, with the stopping of food, the weight drop ceases as in the first, but slower; recurrences are likely with the re-administration of food. Rarely can they be saved by the bottle. In the third stage, very little food increases the symptoms. The breast is the only hope. Functional diagnosis with (1) hunger diet, and (2) test meals is therefore equally dangerous.

Weight.—Food administration causes weight drop, and stopping of food is equally as dangerous, a more paradoxical reaction is hard to imagine. It is important to inquire whether shortly before seeing the patient a rich salt and sugar diet had been changed to a poor one, as this might cause symptoms resembling decomposition.

METABOLISM AND PATHOGENESIS

Decomposition is due to mineral loss. In the fat soap stool stage especially, earthy alkalies are lost, and, with diarrhea stools, leads to much more alkali loss. The increased ammonia in the urine is due to the fact that because of alkali losses ammonia is called on to neutralize the acids in the urine. The increased nitrogen waste results from cell destruction following the withdrawal of salts necessary to their vitality. It is a question whether the salt loss is a primary one, or only secondary to the formation of the acids and a call on them to neutralize the acids. The abnormal acid formation in the intestines is the result of bacterial fermentation of the food stuffs (fat and sugar) through bacterial action. This can only occur where the intestinal epithelium has lost its function, or, at least, been impaired. Heubner first pointed this out.

In the condition of the epithelial cells lies the basis of the difference between decomposition and the simple nutritional disturbances, repair of these cells being difficult or impossible in the former, while recovery is rapid in the simple forms. Pfaundler lays the seat of trouble in the intermediary metabolism, and believes that there is a deep-seated involvement of the organ cells throughout the whole organism.

It remains to be proven in how far the loss of salts is the cause of the clinical picture.

1. Loss of alkalies causes loss of water, as they are necessary to the osmotic equilibrium; the water loss through the skin and lungs is very important, as the loss through urine and bowels equalize one another, and the former losses (skin and lungs) probably account for the weight loss.
2. Loss of alkalies causes destruction of cells.
3. Loss of sodium probably accounts for the subnormal temperature.
4. Loss of sodium probably accounts for the slow heart action. Ringer and Loeb have both shown that sodium stimulates and calcium slows the heart's action.
5. Loss of alkalies results in further acidity of the organism (relative acidosis, according to Steinitz; alkalipenie, according to Ffaundler), of whose rule we know as yet very little in relation to the end result.

The healing quality of mother's milk over cow's milk is undoubtedly due, as shown by the experiments of Meyer, to the difference in the whey content, which has a very good influence in the former, and a deleterious one in the latter, on the impaired epithelium.

PROGNOSIS

The prognosis depends on the following:

1. The stage of decomposition.
2. Feeding of human milk. Even light forms offer little hope with artificial foods.
3. Lowered immunity, which adds danger of infection with colds, bronchitis, etc.

THERAPY

Avoid hunger day and feed human milk, about 200 c.c. daily to start.

1. Feeding with Human Milk.—Must be given in moderate quantity, best guarded by drawing off and feeding, as they drink too rapidly (always hungry), and do not stand large amounts. About 200 c.c. daily is enough to sustain the infants temporarily (60 calories per kilo is sustaining, Rosenstern). (*Erhaltungs Nährung*). Feed often; ten feedings may be given, one every two hours (10 × 20 c.c.); weak tea or saccharin water *ad libitum* between feedings. Expect improvement with the above unless intoxication results from the low salt diet, with resulting loss of water through the stools. If no bad results are seen, increase the food in two or three days. Favorable cases can be fed 100 calories per kilo in ten to fourteen days, and putting to breast may be tried, but the dangers of over-nursing must not be overlooked. Weight may still not improve for some time. (This Keller calls the reparation stage.) This may be shortened by giving one feeding daily of buttermilk or skim-milk, 100 c.c., which is rich in salts and protein. This is not to be done until after the third or fourth week of treatment and with close observation of the result.

Carbohydrates should be added with even greater care. In older children a small amount of farina soup or zwiebach in tea may be tried later.

2. Artificial Feeding.—Change from human to artificial food should always be preceded by a hunger day. After one day of hunger diet small quantities of low fat and sugar diet as buttermilk or skim milk without flour or sugar, or, if not at hand, whey whole or diluted, may be given, using 10 × 10 c.c., and with it saccharin water or tea. Increases must be more careful than with human milk. If results are good, we may increase in two weeks to 70 calories. Add carbohydrates and fats with great care. Carbohydrates increase weight more than fats. Maltose is less likely to affect the bowels and is more assimilable. One per cent. may be added at first, increasing very slowly to 5 per cent. In infants older than 3 months, in addition flour may be used. Always expect a setback with new food additions.

3. Albumin Milk is of value in decomposition where human milk is not available; however, my results would lead me to make every effort in the future to feed this class of infants with human milk. Stimulants, artificial heat, and, in severer types, transfusions are indicated.

V. MIXED FORMS OF NUTRITIONAL DISTURBANCES

Bilanz-Störung (disturbed metabolic balance) is frequently associated with dyspeptic symptoms. Again, these may show signs of intoxication. Decomposition is the form most subject to complication.

THERAPY

Disturbed metabolic balance (*Bilanz-Störung*) with dyspertic symptoms, treat as a dyspepsia by reducing diet. In dyspepsias with signs of intoxication, employ hunger diet, etc.

Decomposition complicated by intoxication is the severest combination, but can be recognized, if careful consideration is given to the history and the infant's general condition. The greatest danger lies in the fact that in the former we must nourish; in the latter starve. Without a hunger day either human or albumin milk should be given in small quantities, 10 × 5 c.c., and increased 50 c.c. daily under control of the clinical symptoms. After eight to ten days of the above the infant can usually be put to the breast five times daily. The weight may remain stationary, and one must judge by the stools and general condition as to the addition of further foods. With albumin milk, after three or four days, the weight becomes stationary and the stools of fat soap character; then gradually some malt sugar can be added.

5514 Indiana Avenue.

METABOLISM AND NUTRITION

Importance of Proper Balance of Fat and Lime in Infant Feeding

(*K. Stolte: Jahrb. f. Kinderh., 1911, lxxiv, No. 4, p. 367*)

Stolte comments on the conflicting statements of various pediatrists in regard to infant feeding, some obtaining excellent results with one food-mixture, while others have found this mixture harmful; some denouncing the very elements in the food to which others ascribe its efficiency. Looking over the entire field from a higher standpoint shows, he says, that one feature is common to all the cases in which the infants thrived, namely, that the stools became less fluid. His research indicates that this change in the consistency of the feces is the result of soap production and absence of fermentation. The aim in feeding, therefore, should be to insure soap production and avoid fermentations. From this standpoint the benefit from the most varied systems of infant feeding is easily understood; each by different routes arrives at the same goal. The essential point is the proper balance of fat and lime in the bowel to insure soap production. If too much or too little of either is present, the desired end is not attained. Fermentations induce the production of fatty acids, which irritate the intestines and interfere with saponification. These views explain the advantages of albumin-milk, as the intestinal flora with this induce putrefaction rather than fermentation. They explain further the tolerance of carbohydrates with buttermilk, which contains especially large proportions of lactic acid and albumin. They also explain how diarrhea may be arrested by albumin-milk, by buttermilk, by diluted milk, or by milk and lime-water. With cow's milk more lime is needed to saponify the fatty acids generated in the intestine by splitting of the fat. Stolte found it possible to check diarrhea almost unfailingly when he gave the infants lime-water with the diluted milk, without carbohydrates. The more complex the structure of the carbohydrate given, the longer it takes to be broken down into its ultimate elements, and thus the less material to ferment in a given period of time, and hence the less opportunity for the fermentation producers to get in their work. These more complex polysaccharids include dextrin, flours and malt. This difference between the various carbohydrates was instructively shown in one of his cases in which the infant had diarrhea on albumin-milk and cane-sugar, while the stools became formed when flour was substituted for the sugar, and the stools became actually hard when nothing but a cereal gruel was given with the albumin-milk. It is possible that the property of promoting putrefaction rather than fermentation is the chief advantage of the albumin-milk. Infants thrive on breast milk after serious illness, although breast milk is poor in albumin, showing that the protein content alone is not the essential factor.

W. T. C.

ACUTE INFECTIOUS DISEASES

Acute Rheumatism Among Children

(*F. Langmead: Lancet, London, 1911, clxxxi, 1133*)

Altogether 2,556 children were examined by Langmead. Of these, 844 were boys and 838 girls in the senior departments, i. e., from 6½ to 14 years old; 874 were attending the infants' department, and consisted of nearly equal numbers of boys and girls from 3 to 6½ years old. Fifty-nine boys and 74 girls could be classified as definitely rheumatic, a total of 133. This is equivalent to a percentage incidence of 5.20 for children of all ages attending school, or of 6.83 for children in the senior departments only, those attending the infants' department being excluded from the estimation. In the majority of cases attention was drawn to the rheumatic child by the condition of the heart, sometimes by definite valvular disease, at others by dilatation accompanied by such alteration in sounds and rhythm as one is accustomed to hear in rheumatic children. More and more children become rheumatic as they grow older. There is, however, an apparent accession of rheumatism at the age of 10 which is not shown in subsequent years. Langmead gives no explanation for this and regards it as an inaccuracy which would have disappeared if a large enough number of children had been examined.

Out of these 133 children all except eighteen showed some evidence of cardiac disorder at the time of examination. Thus rheumatic heart affections occurred in 4.49 per cent. of the children of all ages attending school, or in 5.94 per cent. of those in the senior departments only. Obvious valvular disease was found in 2.93 per cent. of children at all ages, or 3.92 per cent. of those in the senior departments. Mitral regurgitation was noted forty-four times; aortic regurgitation and mitral stenosis only once; dilatation with a systolic bruit at the apex, possibly mitral regurgitation, twelve times; dilatation with a short presystolic rumble, or so-called reduplicated second sound (mid-diastolic bruit), possibly early mitral stenosis, eight times; dilatation without bruits, twenty times. The comparative rarity of aortic regurgitation in children is emphasized by the fact that only one case was discovered among the 2,556 children examined. Chorea did not appear among the children or in the histories of their previous illnesses as often as might have been expected. There were eighteen cases only, which amounted to 0.70 per cent. of the children of all school ages or 1.06 per cent. of the children in the senior departments. The comparative incidence in boys and girls followed the usual rule, there being twice as many girls affected as boys. Thus 0.71 per cent. of the boys were at some time choreic and 1.43 per cent. of the girls. The relation of enlarged tonsils and adenoid vegetations to rheumatism in childhood is well illustrated by the figures obtained. Taking the 133 rheumatic cases, in seventy-five there were no signs of abnormality in the throat, in twenty-one the tonsils were slightly enlarged, in eleven considerably enlarged, in sixteen greatly enlarged and in three tonsillotomy had been performed before the patients were examined. Adnoids were responsible for producing signs of post-nasal obstruction and mouth-breathing in seven. In other words, there was an abnormality of the tonsils or pharyngeal mucosa or both in fifty-eight cases, or in 43.6 per cent. of the rheumatic cases. This was sufficient to warrant operative interference in thirty-seven cases, or 27.8 per cent. of the rheumatic cases. F. C. ZAPFFE.

Diphtheritic Paralysis

(*Andrew Love: Glasgow Med. Jour., 1911, x, 245*)

The cases on which this article is based were under Love's care in Belvidere Fever Hospital, Glasgow, during the years 1900-1906, inclusive, and in Gateside Fever Hospital, Greenock, during the years 1908-1911, inclusive. The number of cases of diphtheria admitted during the period selected was 1,313, and of these eighty-five or roughly 6 per cent. became paralyzed. The years 1905 and 1906, and more especially 1906, show an enormous increase in the number of cases of paralysis. This was principally due to the greater severity of the disease during these years. Of the total number of cases observed who suffered from paralysis, thirty-four were males and fifty-one females, their ages ranging between 14 months and 40 years. Paralysis was more common at those ages when the incidence of the disease is greatest. Generally speaking, the later the day of illness before antitoxin is administered the greater is the toxemia, and naturally, the greater the danger of paralysis supervening. Of these eighty-five patients, sixty-five, or 77 per cent., recovered, and twenty, or 23 per cent., died. In no one case could death be attributed solely or directly to paralysis, although in all cases it was contributory. In ten of the cases that terminated fatally the disease was of the malignant type, while in the others it was of a severe character. Eight had nasal implication, seven a combination of faucial and laryngeal diphtheria with tracheotomy in three instances, and twenty-seven had greatly enlarged cervical glands. Of the latter, two went on to suppuration. Of the eighty-five cases, fifty-three, or almost two-thirds, had paralysis of the palate alone; fifteen of the eyes and palate; three of the eyes alone (strabismus). Of the fifteen who were afflicted with paralysis of the eyes and palate combined, three had paralysis of accommodation as well as strabismus. Paralysis of the ocular muscles alone is uncommon, and only two of the sixty-eight patients recorded were affected in that way. Of the twelve patients noted as having intercostal and cardiac paralysis, nine died and three recovered, the main symptoms being great difficulty in inspiration with marked feebleness and irregularity of the heart. In the one case in which the lower limbs only were affected the loss of power lasted only for a few days. The average duration of the paralysis was eighteen days. Two of the cases had paralysis of the palate on admission to the hospital, and the condition persisted until death occurred. In the cases in which death occurred the average number of days of residence in hospital was twenty-one, while the average number of days spent in hospital by those who recovered was 70.5. It is interesting also to note the persistence of the membrane on the throat after the administration of antitoxin. In no instance did the membrane disappear before the third day after admission to hospital, and only then in the milder cases. The average number of days that elapsed in the cases here recorded before the throat was free from membrane was 7.2; the longest period noted during which the membrane persisted was fourteen days. Vomiting in diphtheria is always regarded with apprehension, as it is frequently associated with cardiac failure. In the cases here recorded vomiting occurred in fourteen, and nine of these had a fatal termination. It is noteworthy that the vomiting occurred simultaneously with the onset of the paralysis. The urine varied greatly as regards albumin. Of the eighty-five cases, twenty-seven had a large quantity of albumin in the urine, eighteen a moderate quantity, seventeen a mere trace, and twenty-three no albumin at all. With one exception there was a large quantity of albumin in the urine of all the fatal cases. In the cases under consideration fifty-six received a single dose of antitoxin, the smallest being 6,000 units and the largest 75,000 units, while the average amount administered was 17,000 units. Second doses were given in twenty-four cases, the average in these being 17,500 units. In five cases only were third doses resorted to, the average in these instances being 9,500 units. The over-all average, that is, the average aimed at by taking all the doses administered to all the patients, is represented by the somewhat large amount of 22,000 units. In connection with the administration of antitoxin, it is interesting to note that out of the eighty-five cases dealt with, thirty-eight were afflicted with serum rashes. In twenty-eight cases the rash was urticarial in character and general in distribution; in six it was scarlatiniform, and in four morbilliform. Two of the rashes, which on their first appearance were urticarial, became morbilliform in about twenty-four hours, while one, which was in the first instance scarlatiniform, became morbilliform in the same time. The serum rash when urticarial in character appeared usually on the ninth day after the administration of serum, and lasted on an average 4.2 days. The scarlatiniform rash also appeared on the ninth day, but usually lasted only two days, while the morbilliform rash came out on the twelfth day after the injection of serum, and as a rule lasted four days. All important as is the early administration of antitoxin, it is a mistake to suppose that in the late cases antitoxin is of no avail. Twenty-seven of the patients were admitted after the fifth day, and all received antitoxin. Of these, five died, a mortality of 18.5 per cent.

F. C. Zapffe.

Blood-Pressure in Diphtheria

(*J. D. Rolleston: Brit. Jour. Child. Dis., 1911, x, 433*)

This paper is based on observations made on 179 cases of diphtheria admitted to the Grove Hospital from July, 1909, to December, 1910. The blood-pressure in each case was taken with C. J. Martin's modification of Riva-Rocci's sphygmomanometer. The systolic pressure, as measured by disappearance of the radial pulse, was alone taken into consideration. As far as possible the measurements were taken at the same time each day between 10:30 a. m. and noon; i. e., from one and one-half to five hours after food; in many cases an evening record between 6:30 p. m. and 7 p. m. was also made. The blood-pressure was taken daily in each case until the patient was allowed to sit up; i. e., for a period ranging from three weeks in the mild cases to six or eight weeks in the severe. Comparative observations were subsequently made on the different readings in the recumbent and erect positions. Apart from the early fatal cases the total period of observation in each case ranged from four to fourteen weeks. All the patients, except fifteen who were above the age of 15 years, were children. Ninety were males, eighty-nine were females. There was no appreciable difference in the blood-pressure of any two individuals of different sexes but of the same age and suffering from attacks of diphtheria of equal severity. Of the 179 cases, sixty-three, or 35.1 per cent., according to Cook and Brigg's estimate, and forty-five cases, or 25.1 per cent., as judged by Seiler's standard, showed for varying periods a pressure inferior to the normal. Owing to the well-known depressive effects of diphtheria toxins these figures appear surprisingly low, but are explained by the inclusion of a large number of mild cases, in which the blood-pressure was not lowered in the course of their illness. The varying degrees of depression bore a direct relation to the severity of the attack, being pronounced and persistent in the severe and slight and transitory in the mild cases. Of those whose blood-pressure was not lowered, thirty-six cases, 20.1 per cent., according to Seiler's standard, showed a reading which always exceeded the normal. Judged, however, by the more liberal estimate of Cook and Briggs, the pressure of these cases did not persistently rise above the normal limits. In ninety-seven of the 130 cases admitted in the first week of disease and in ten of the fifteen cases admitted in the second week, the highest reading was the first taken. The occurrence of the comparatively high pressures in the first week is attributed partly to the febrile disturbance of the acute stage before the diphtheria toxins had had time to produce their characteristic effect and partly to the psychical action caused by the application of an unfamiliar instrument, the latter fact accounting for the highest reading being usually obtained on the first measurement. The preponderance of the lowest readings in the second week accords with the clinical fact that this is the time of predilection for the so-called "cardiac paralysis," which should more accurately be called vasomotor paralysis, the heart failure being secondary to the vasomotor affection. Apart from one case of diaphragmatic paralysis, all the deaths in the present series were due to this cause. The lowest reading in a patient who recovered was 60 mm., which was registered on one occasion in a girl aged 3 years. In only ten other patients who recovered did the pressure fall below 80 mm. in patients above the age of 2 years. The pressure in forty cases returned to the normal by the end of the seventh week. Forty-two cases, or 23.4 per cent., showed various degrees of laryngeal involvement. In thirteen severe cases tracheotomy was performed; in eleven moderate cases the symptoms, though fairly well marked, did not require surgical interference: in eighteen mild cases the laryngeal symptoms consisted merely of a croupy cough and husky voice, thus representing the first degree of croup of earlier writers. The effect of laryngeal obstruction on the blood-pressure was most marked in the severe cases. Increase in dyspnea was followed by a rise of pressure and the relief of the obstruction on opening the trachea was immediately followed by a considerable fall. The rise of blood-pressure in the moderate laryngeal cases was less than in the severe. The blood-pressure in the mild laryngeal cases during the acute stage was not any higher than in the purely faucial cases; in fact, it may be said to have been dominated by the character of the concomitant faucial attack. In the great majority of early serum rashes, erythematous or urticarial, no change occurred in the pressure, while in a large percentage of late eruptions, which are usually associated with febrile disturbance and often with pains in the joints, muscles and fasciæ, the pressure was raised. Thus of seventy-seven cases at the time of the early eruption, sixty-two patients, or 80.5 per cent., showed no change in the pressure, in nine it was raised and in six it was lowered. On the other hand, out of fifty with late rashes, in twenty cases, or 40 per cent., the pressure was raised, in twenty-eight, or 56 per cent., there was no change, and in only two cases, or 4 per cent., it was lowered. The rarity of any rise in pressure at the time of the early rash is in keeping with the fact that during the second week of the disease, in which most of these rashes occur, the pressure is usually at its lowest. In the third week, in the course of which the late serum phenomena occur, the pressure as a rule is no longer falling, while on the other hand the fever and joint pains tend to raise it. As arterial hypotension and albuminuria are both phenomena of diphtheritic intoxication, any change in the blood-pressure coexistent with the occurrence of albuminuria was almost invariably in a downward direction. Thus among fifty-one cases in whom albuminuria was not present on admission, its onset was accompanied by a fall in the pressure in twenty-six and in twenty-five there was no change; in another eight cases increase of preexistent albuminuria was accompanied by a fall in the pressure. The solitary exception to the rule occurred in a girl aged 6 years, in whom severe faucial diphtheria was complicated on the twenty-ninth day by uremic convulsions, one of the rarest events in diphtheria. On the two following days the blood-pressure, which up till then had not been examined, stood at the disproportionately high figure of 120 mm., falling on the thirty-second day to 80 mm. Death took place on the thirty-third day. Albuminuria in diphtheria thus offers a striking contrast to scarlatinal albuminuria, during which it is usual for the blood-pressure to be raised. Thus in eleven such cases Rolleston found a rise in all but two. In early paralysis the blood-pressure tended to fall. In late paralysis, even when extensive, it was usually not affected. Rolleston concludes that sphygmomanometry in diphtheria, as in other acute diseases, though of considerable theoretical interest, has little practical significance.

F. C. Zapffe.

TUBERCULOSIS AND SYPHILIS

Consumption and Order of Birth

(*W. C. Rivers: Lancet, London, 1911, clxxxi, 987*)

Rivers observed in patients' case-sheets which showed ordinal position in the family, a large number of entries of eldest-born children, and from this observation conceived the idea that clinical pulmonary tuberculosis might affect such persons more than others. Brehmer's and Riffel's reports show that both first- and second-born offspring appear subject to consumption at a very much higher rate than younger members of a family. Rivers' own observations in 263 cases confirm those of other clinicians. Mitchell, among 443 idiots and imbeciles, found 138 first-born, or 31.1 per cent. Langdon Down claims liability to idiocy among primiparous children because 24 per cent. of the 2,000 idiots (illegitimate largely excluded) examined by him were first-born children. Among Wilbar's 675 there were 191 first-born; among 100 of Beach's, twenty. Thus, respecting the exact amount of increased risk of developing phthisis that an eldest child runs, no direct data exist from which to calculate. As matters stand, one may say that whereas in 1,228 consumptives (494 upper middle-class Germans; 353 middle- and lower-class inhabitants of Lancashire, London, and Northumberland, and 381 mainly lower-class Lancastrians) one should find 196 eldest children, one actually does find 281, i. e., eldest-born consumptives are in excess, say, 40 per cent.

Of 141 of Rivers' last cases there is one patient with diabetes mellitus, three who suffer from hay fever, and three the subjects of congenital xerodermia. The diabetes patient is an eldest child; two of the hay fever patients are likewise, while the remaining one is second-born, and two of the ichthyotics are eldest-born. Yet the first- and second-born of these 141 only number fifty-eight and the first-born alone only twenty-eight. This, in Rivers' opinion, would seem to point to the conclusion that the tendency of the eldest-born to become consumptive is an innate tendency and the hypothesis is strengthened, he says, if we appeal to the literature of the subject. Lunatics and idiots are certainly very liable to consumption, and, as has been seen, it is exceedingly likely that they are disproportionately often eldest-born. Again, if faulty upbringing by inexperienced parents is to be made responsible for elder-born criminals, lunatics, idiots and perhaps men of genius, this would render ordinary human responsibility sufficiently formidable. The existing evidence negatives the view that infection is the sole cause.

F. C. Zapffe.

TRANSMISSION OF DISEASE BY MEANS OF BOOKS

Request for Data

I am preparing a paper on "Books as a Source of Disease," to be read before the next International Congress on Hygiene, and in order to obtain data, I respectfully request the readers of this note to send me an account of any cases, the sources of which have been traced to books or papers, or where the evidence seemed to make books or papers the offender. I further request information concerning cases in which illness or even death has been caused by the poisons used in book-making.

All the information possible is wanted in order to present as complete a paper as possible. As in the case of insects which we now know to be "carriers of disease," it is first necessary to collect the scattered evidence in order to show that there is real danger in books; and this will compel better care to be taken of libraries and books and improve the health of mankind.

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William R. Reinick,
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BOOK REVIEW

Case Histories in Pediatrics. A Collection of Histories of Actual Patients Selected to Illustrate the Diagnosis, Prognosis and Treatment of the Most Important Diseases of Infancy and Childhood. By John Lovett Morse, A.M., M.D., Assistant Professor of Pediatrics, Harvard Medical School; Associate Visiting Physician Infant's Hospital and Children's Hospital, Boston. W. M. Leonard, Boston, Mass., 1911.

The title of this volume describes its purpose and mission. Teaching medical students by means of actual case histories originated at Harvard several years ago. The author states in his preface that this method of teaching is far superior to recitations, quizzes and conferences. It compels the student to think for himself. It is almost as valuable as the clinical lecture, in which the patient is shown, and is more instructive than the didactic lecture.

This book should inspire every physician who teaches any branch of clinical medicine to follow out the same method with his own cases. The description of each case is so clear and concise and the essential points in the examination and diagnosis so forcibly brought out that this little volume could well serve as a pattern.

There are one hundred cases cited, which are grouped into Diseases of the New-Born, Gastro-Intestinal Tract, Nutrition, Infectious Diseases, etc. Each case illustrates a different disease, except in a few instances, wherein two examples which illustrate different phases of the same disease are included.

The value of this book would be greatly enhanced if more illustrative cases were included under certain sections. It is impossible to give a comprehensive picture of diseases such as tuberculous meningitis, bronchopneumonia, etc., by quoting one case.

The omission of cases illustrating chorea, tuberculosis, asthma, enuresis and the acute exanthemata, which are important and characteristic diseases of childhood, should be remedied in later editions.

The discussion of the differential diagnosis is full of practical points which the author has gleaned from his own wide personal experience. The treatment is based on what was needed and undoubtedly advised in each individual case.

There is nothing in this volume that savors of the text-book. The general practitioner will find many valuable suggestions and useful hints which are not found in other books. The index is complete and reference to the various diseases can readily be made.

The book would be more readable and satisfactory from a typographical point of view if the name of the disease were printed prominently as a heading to each case.

INDEX TO VOLUME II

PAGE
Accessory sinus suppuration in scarlatina 11
Acid control of pylorus in infants 252
Acid, hippuric, in urine of normal breast-fed infants 248
Albumin milk in infant feeding 180
Amberg, S.: Hippuric acid in urine of normal breast-fed infants 248
Anaphylaxis in relation to pediatrics 39
Apparatus for collection of infants' excreta 415
Arteries and veins 360
Atrophic infants, fat absorption in 21

Bacillus acidophilus, a study of its possible therapeutic use 30
Bed, metabolism, for infants 419
Birth, order of, and consumption 448
Blood-pressure in acute nephritis of children 62
Blood-pressure in paralysis 447
Books, transmission of disease by means of 449
Boston's Hospital School for tuberculous children 286

Carbohydrates in creatin-creatinin metabolism 366
Case histories in pediatrics; book review 449
Casein curds in infants' stools 146
Casein in infant feeding 315
Consumption and order of birth 448
Cooke, R. A.: Metabolism bed for infants 419
Correspondence, Brem's paper on influenzal meningitis 63
Councilman, W. T.: Myatonia congenita 340
Cowie, D. M.: Acid control of the pylorus in infants 252
Creatin-creatinin metabolism, carbohydrates in 366
Creatin, excretion of, in infancy and childhood 367

Dixon, S. G.: Epidemiologic and etiologic studies of acute poliomyelitis in Pennsylvania 221
DuBois, E. F.: An apparatus for collection of infants' excreta 415
Dunn, C. H.: Myatonia congenita 340

Edebohls' operation in chronic nephritis in children 267
Endocarditis 358
Excreta, infants', apparatus for collecting 415

Fairbanks, A. W.: A case of scaphocephalus with retinal changes 149
Fat absorption in atrophic infants 21
Fat and lime in infant feeding, proper balance of 444
Fife, C. A.: Studies in the metabolism of atrophic infants 19
Fleischner, E. C.: Relation of meat ingestion to indicanuria in children 262
Flexner, S.: The control of epidemic poliomyelitis 96
Freeman, R. G.: Intestinal infantilism of Herter 332

PAGE
Glands, lymphatic, in scarlatina, bacteriologic examination of............ 329
Glands, salivary, enlarged, lymphatic leukemia in a child with............ 293
Graham, E. E.: Pyloric stenosis in older children with report of a case of pyloric spasm ending fatally.................................... 407
Grulee, C. G.: Albumin-milk in infant feeding......................... 180

Heart-block 357
Heart disease, congenital 356
Herter, intestinal infantilism of...................................... 332
Hess, J. H.: Disturbances of nutrition of the artificially fed infant with practical application of the classification of Finkelstein.............. 422
Hess, J. H.: Study of the caloric needs of premature infants.............. 302
Hoobler, B. R.: The rôle of mineral salts in the metabolism of infants..... 107
Howland, J.: Metabolism bed for infants.................................. 419
Howland, J.: The fundamental requirements of an infant's nutrition....... 49
Hubbard, T.: Accessory sinus suppuration in scarlatina................. 11

Indicanuria and meat ingestion in children............................. 262
Indicanuria in new-born.. 289
Indigestion, chronic intestinal... 61
Infancy, excretion of creatin in.. 367
Infant, artificially fed, disturbances of nutrition of..................... 422
Infant feeding, malt sugar and casein in................................. 315
Infant feeding, proper balance of fat and lime in........................ 444
Infantile paralysis 141
Infantile paralysis, abortive type of..................................... 92
Infantile paralysis, cerebral forms of.................................... 75
Infantile paralysis, epidemic, control of................................. 96
Infantile paralysis in Massachusetts in 1910............................ 145
Infantile paralysis, notice in regard to...............................55, 212
Infantile paralysis, occurrence of, in Massachusetts in 1907-1910.......... 369
Infantile paralysis, occurrence of in the United States and Canada in 1910.. 65
Infantile paralysis, outlook for improvement of treatment in............. 102
Infantile paralysis, polyneuritic type.................................... 92
Infantile paralysis, progressive type..................................... 92
Infantile paralysis, spinal form.. 92
Infantilism, intestinal, of Herter.. 332
Infants, acid control of pylorus in....................................... 252
Infants, atrophic, studies in metabolism of................................ 19
Infants, excreta of, apparatus for collecting.............................. 415
Infants, metabolism bed for... 419
Infants, normal breast-fed, hippuric acid in urine of...................... 248
Infants, premature, caloric needs of...................................... 302
Infants, relationship of gastric to pancreatic fat digestion in............. 243
Infection of the new-born, a case of..................................... 210
Influenzal meningitis, correspondence concerning a correction in Brem's paper 63
Intestinal flora of children, influence of sugar on........................ 58
Intussusception in children.. 61
Intussusception in children, treatment of................................. 60

Karsner, H. T.: Epidemiologic and etiologic studies of acute poliomyelitis in Pennsylvania 221

PAGE
Kendall, A. I.: A preparatory study of the bacillus acidophilus in regard to its possible therapeutic use 30
Kidney diseases 361
Knox, J. H. M., Jr.: Hippuric acid in urine of normal breast-fed infants 248
Knox, J. H. M., Jr.: Infantile paralysis: outlook for the improvement of treatment in 102
Kolmer, J. A.: Bacteriologic examination of lymphatic glands in scarlet fever 329
Koplik, H.: Cerebral forms of poliomyelitis 75
Koplik, H.: Treatment of chronic nephritis in children by the Edebohls operation 267

Leukemia, lymphatic, in a child with marked enlargement of salivary glands. 293
Lime and fat in infant feeding, proper balance of 444
Lovett, R. W.: Infantile paralysis in the United States and Canada in 1910 .. 65
Lovett, R. W.: Infantile paralysis with especial reference to its occurrence in Massachusetts, 1907-1910 369
Lyon, W.: Acid control of the pylorus in infants 252

Malt sugar and high percentages of casein in infant feeding 315
Measles, cytologic and clinical observations on the incubation period of 213
Meat ingestion and indicanuria in children 262
Meningitis, epidemic cerebrospinal 281
Meningitis in infancy 59
Metabolism bed for infants 419
Metabolism, creatin-creatinin, carbohydrates in 366
Metabolism in infants, rôle of mineral salts in 107
Metabolism of atrophic infants, studies in 19
Metabolism, protein, in infants and children 189
Migraine in children due to disturbances of function of thyroid gland 62
Mikulicz' disease 293
Mineral salts in the metabolism of infants 107
Morse, J. L.: Infantile paralysis: spinal form 92
Morse, J. L.: Use of malt sugar and high percentages of casein in infant feeding 315
Myatonia congenita 340
Myocarditis 358

Nephritis, chronic, in children, treatment of, by Edebohls' operation 267
Nephritis in children, blood-pressure in 62
New-born, a case of infection of 210
New-born, indicanuria in 289
Nicoll, M.: Treatment of sepsis in scarlatina with antistreptococcus serum .. 1
Nitrogen metabolism in atrophic infants 25
Nutrition and growth 147
Nutrition, fundamental requirements of an infant's 49
Nutrition of artificially fed infants, disturbances of 422

Ordway, T.: Muscular hypertrophy of the pylorus in infancy 159

Paralysis, blood-pressure in 447
Paralysis, diphtheritic 445
Paralysis, infantile, occurrence of, in Massachusetts in 1907-1910 369
Pease, M. C.: Anaphylaxis in its relation to pediatrics 39

PAGE

Pericarditis 358
Pisek, G. R.: Anaphylaxis in relation to pediatrics 39
Poliomyelitis 141, 367
Poliomyelitis, acute, epidemiology and etiology of, in Pennsylvania 221
Poliomyelitis, cerebral forms of 75
Poliomyelitis, epidemic, control of 96
Poliomyelitis, epidemic, notice in regard to 55
Poliomyelitis, occurrence of, in Massachusetts, in 1907-1910 369
Protein metabolism in infants and children 189
Pylorus, infant's, acid control of 252
Pylorus, muscular hypertrophy of, in infancy 159
Pylorus, spasm of, case of, ending fatally 407
Pylorus, stenosis of, in older children 407

Rheumatism, acute, among children 445
Richardson, M. W.: Infantile paralysis with especial reference to its occurrence in Massachusetts, 1907-1910 369
Rotch, T. M.: A preparatory study of the bacillus acidophilus in regard to its possible therapeutic use 30

Salvarsan in syphilis in childhood 60
Scaphocephalus with retinal changes 149
Scarlatina 219
Scarlatina, accessory sinus suppuration in 11
Scarlatina, bacteriologic examination of the lymphatic glands in 329
Scarlatina, streptococci in 290
Scarlatina, treatment of, with antistreptococcus serum 1
Schlutz, F. W.: Relationship of gastric to pancreatic fat digestion in infants 243
School inspection in small towns 55
Schwarz, H.: Protein metabolism in infants and children 189
Sedgwick, J. P.: Relationship of gastric to pancreatic fat digestion in infants 243
Sepsis in scarlatina, treatment of, with antistreptococcus serum 1
Shaw, H. L. K.: Muscular hypertrophy of the pylorus in infancy 159
Streptococci in scarlet fever 290
Sugar, influence of, on intestinal flora of children 58
Syphilis, inherited 368

Tayler-Jones, L.: A case of infection of the new-born 210
Thymus gland, newer investigations on and their importance for pediatrics.. 56
Thyroid gland, migraine due to disturbances of 62
Tileston, W.: A discussion of Mikulicz' disease with report of a case of lymphatic leukemia in a child with marked enlargement of the salivary glands 293
Tuberculosis and order of birth 448

Urine of normal breast-fed infants, hippuric acid in 248

Veeder, B. S.: Studies in the metabolism of atrophic infants 19
Veins and arteries 360

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